Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

**DRAFT RISK ASSESSMENT OF A BIOCIDAL PRODUCT (FAMILY) FOR NATIONAL AUTHORISATION APPLICATIONS**

(submitted by the evaluating Competent Authority)



FAMILLE JUVA REPULSIF INSECTES

Product type(s) 19

Ethyl butylacetylaminopropionate – IR3535®

Case Number in R4BP: BC-ET020532-37

Evaluating Competent Authority: France

Date: 30th May 2018

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**Note to the reader**

This consolidated PAR for the product authorisation of FAMILLE JUVA REPULSIF INSECTES is based on the PAR of the first authorisation, in which post-authorisation data assessment have been included.

1. **History of the dossier**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Application type** | **refMS** | **Case number in the refMS** | **Decision date** | **Assessment carried out (i.e. first authorisation / amendment /)** |
| NA-APP | FR CA | BC-ET020532-37 | 30/05/2018 | First authorisation |
| NA-APP | FR CA | - | - | Post-Autorisation data assessment |

# CONCLUSION

The biocidal family product (BFP) FAMILLE JUVA REPULSIFS INSECTES contains two meta SPC.

The meta SPC 1 contained initially 2 products (for textile and skin application). The product for textile application has been deleted by the applicant during the assessment. Therefore, the meta SPC 1 contains one single product. It is an aerosol (AE) formulation intended to be used by spraying on skin by adults and infants > 3 years against adults mosquitoes (*Aedes spp., Anopheles spp and Culex spp*) and adults sandflies (*Phlebotomus spp*).

The meta SPC 2 contains five single products. They are liquids formulations intended to be used indoor and outdoor by spraying on skin adults and infants > 3 years against mosquitoes (*Aedes SP, Anopheles Sp and Culex Sp- adults*), sandflies *(Phlebotomus sp; adults*) and ticks (*Ixodes*-nymphs and adults).

**Conclusion on physico-chemical properties and analytical methods**

Regarding the physico-chemical properties for the family product FAMILLE JUVA REPULSIFS INSECTES, all studies have been performed in accordance with the current requirements and the results are deemed to be acceptable except for the accelerated storage stability meta SPC 1.

The appearance of product for the meta SPC 1 is an homogeneous limpid liquid colourless. There is no effect of high temperature on the stability of the formulation, since after 8 weeks at 40°C, neither the active ingredient content nor the technical properties were changed. The stability data indicate a shelf life of at least 2 years at ambient temperature when stored in aluminium bottle packaging material (commercial packaging material).

For the meta SPC 2, the appearance of the product is an homogeneous limpid liquid colourless. There is no effect of high temperature on the stability of the formulation, since after 8 weeks at 40°C, neither the active ingredient content nor the technical properties were changed. The stability data indicate a shelf life of at least 2 years at ambient temperature (do not expose to temperatures exceeding 40°C and lower than 0°C) when stored in HDPE bottle packaging material (commercial packaging material). The long term storage stability study (36 months) is on-going.

The analytical methods for meta SPC 1 and meta SPC 2 are fully validated.

Data required for meta SPC 1 and meta SPC 2: The studies of long term storage should be provided within two years.

**Conclusion on efficacy**

French competent authorities (FR CA) conclude that data :

* Product from the Meta SPC 1 (one formulation without any variations) of the BPF JUVA répulsif insectes provides a protection time up to 7 hours against adult mosquitoes (*Culex spp*., *Aedes spp*. *Anopheles spp*.) and sandflies (*Phlebotomus spp*.).
* For the meta SPC 2, the product “Marie Rose Spray anti-moustiques – Référence 096602” insects provides a protection time up to 6.5 hours against adult mosquitoes (*Culex spp., Aedes spp. Anopheles spp*.) and sandflies (*Phlebotomus spp*.) and, up to 6 hours against adults and nymphs of the tick *Ixodes ricinus*. Variations of composition within meta-SPC2 are considered as limited and FR CA proposes to authorize the meta SPC 2.

It is to be noted that no claim has been made concerning efficacy on tropical tick species, the efficacy of this product against ticks in tropical areas is not demonstrated.

**Conclusion on human health**

Considering the intended uses on human skin of FAMILLE JUVA REPULSIFS INSECTES, conclusions regarding risks for human health are the following:

Meta SPC 1 (product to be used against mosquitoes and sandflies)

* two applications per day (as claimed by the applicant) lead to unacceptable risk
* the risk is acceptable for adult and children from 3 years for one application per day only.

Meta SPC 2 (product to be used against mosquitoes, sandflies and ticks):

* for the application of the product against mosquitoes and sandlies, the risk is acceptable for adult and children from 12 years for two applications per day. The risk for children between 3 and 11 years is acceptable for one application per day.
* for the application of the product against ticks, the risk is acceptable for adult and children from 3 years for one application as claimed by the applicant.

***IN FRANCE ONLY***

Given the risk of vector-borne diseases transmission in France, FR CA considers that the biocidal familly products FAMILLE JUVA REPULSIFS INSECTES can be authorized for application on humans, with appropriate risk mitigation measures that limit human exposure based on article 19(5). The following RMMs are considered as applicable in France:

* For adult: “apply on the head, neck, hands, ¾ arms, ½ legs once a day”
* For children: “do not apply the product on hands of children” and ““apply on the head, neck, ¾ arms, ½ legs once a day”

Meta SPC 1:

With these additional RMMs, the risk for human health is acceptable for adult and children from 12 years old for two applications per day and for children between 3 and 11 years old for one application only. Due to the need to protect children from vector-borne diseases product will be authorized for two applications per day for children between 3 and 11 years old in risk areas, as it is authorized for adults.

Meta SPC 2:

With these additional RMMs,

* for the use against mosquitoes and sandflies the risk is acceptable for adult and children from 12 years old for two applications per day. The risk for children between 3 and 11 years is acceptable for one application. However, due to the vector-borne diseases and the presence of voectors all around the day and possiby at night, two applications per day for children between 3 and 11 years old will also be authorized in risk areas, as it is authorized for adults.
* For the use against ticks, , the risk is acceptable for adult and children from 3 years for one application per day.

**Conclusion on indirect exposure via residues in food**

Regarding the intended use on skin of the BPF FAMILLE REPULSIF JUVA INSECTES, a contamination of food cannot be excluded.

An estimation of dietary exposure for toddlers, children and adults was performed. These estimations are considered as a worst case using the assumption that all the active substance from the palm hands will be ingested. According to use recommendations and risk mitigation measures, no dietary risk was identified for children and adults considering the directions for use: Avoid any direct or indirect contact with food and feed.

**Conclusion on ecotoxicology and environment**

The use of the BFP FAMILLE REPULSIF JUVA INSECTES does not induce risk for any of the environmental compartments.

**Overall conclusion**

**The efficacy of the product is demonstrated against mosquitoes sandlies and ticks when applied on human skin. Considering that 55 % of the body is exposed (Head-hoc recommendation n°14), the risk for human health is unacceptable for méta SPC 1 when the product is applied maximum twice per day. Therefore conditions of article 19.1.b) iii) are not met for this intended uses of the biocidal family FAMILLE JUVA REPULSIFS INSECTES. The risk is however acceptable for méta SPC 1 when the product is applied maximum once per day and for the meta SPC 2 according to the entended uses claimed by the applicant.**

**In France, given the risk of vector-borne diseases transmission, FR CA considers that the biocidal familly product FAMILLE JUVA REPULSIFS INSECTES can be authorized for application on humans, based on article 19(5), with appropriate risk mitigation measures that limit human exposure. Following appropriate risk mitigation measures indicated in the SPC,**

* **products from FAMILLE JUVA REPULSIFS INSECTES against mosquitoes and sandlies can be applied up to twice per day on adults and on children from 3 years old;**
* **products from meta SPC 2 of FAMILLE JUVA REPULSIFS INSECTES to be used against tick can be applied once per day on adults and on children from 3 years old. Only uncovered parts of the body shall be treated, limited to head, ¾ arm, hand (adult only) and ½ legs**

* **Post authorisation data – FAMILLE JUVA REPULSIF INSECTES – 2021 :**

Shelf life study reports for META SPC 1 and META SPC2 were provided.

Long term storage study shows that META SPC1 product remains stable after 3 years at 30°C in aluminium packaging.

Long term storage study shows that META SPC2 product remains stable after 3 years at 20°C in HDPE or PP packaging.

# ASSESSMENT REPORT

## Summary of the product assessment

**Part I.- First information level**

**1-Administrative information**

**1.1 Identifier of the product / product family**

| **Identifier[[1]](#footnote-1)** | Country (if relevant) |
| --- | --- |
| **Famille Juva répulsif insectes** | France |

**.1.2 Authorisation holder**

|  |  |  |
| --- | --- | --- |
| **Name and address of the authorisation holder** | Name | Laboratoires Juva Santé |
| Address | 8 rue Christophe Colomb  75008 Paris, France |

**1.3 Manufacturer(s) of the products of the family**

|  |  |
| --- | --- |
| **Name of manufacturer** | Laboratoires Juva Santé |
| **Address of manufacturer** | 8 rue Christophe Colomb  75008 Paris, France |
| **Location of manufacturing sites** | Laboratoires Juva Production  Rue Avogadro  Technopole Forbach Sud  57600 Forbach, France  TUNAP Cosmetics  Bahnhofstraße 47  6175 Kematen in Tirol, Austria |

**1.4 Manufacturer(s) of the active substance(s)**

|  |  |
| --- | --- |
| **Active substance** | IR3535®, Ethyl butylacetylaminopropionate, ethyl N-acetyl-N-butyl-β-alaninate (EINECS) |
| **Name of manufacturer** | Merck KGaA  Merck S.L.U. |
| **Address of manufacturer** | Merck KGaA  FranckfurterStrasse 250  64293 Darmstadt – Germany  Merck S.L.U.  Calle Maria de Molina  28006 Madrid - Spain |
| **Location of manufacturing sites** | Merck S.L.U.  Poligono Merck  08100 Mollet de Valles (Barcelona) - Spain |

**2 Product (family) composition and formulation**

NB: the full composition of the product according to Annex III Title 1 is provided in the confidential annex.

Does the product have the same identity and composition as the product evaluated in connection with the approval for listing of the active substance(s) on the Union list of approved active substances under Regulation No. 528/2012?

Yes

No

**2 .1 Identity of the active substance**

|  |  |
| --- | --- |
| Main constituent(s) | |
| ISO name | IR3535®, Ethyl butylacetylaminopropionate, ethyl N-acetyl-N-butyl-β-alaninate (EINECS) |
| IUPAC or EC name | ethyl 3-[N-acetyl-N-butyl] aminopropionate |
| EC number | 257-835-0 |
| CAS number | 52304-36-6 |
| Index number in Annex VI of CLP |  |
| Minimum purity / content | > 99 % w/w |
| Structural formula |  |

**2.2 Candidate(s) for substitution**

The active substance IR3535 is not candidate for substitution in accordance with Article 10 of BPR–Regulation 528/2012.

**2.3 Qualitative and quantitative information on the composition of the biocidal product family2**

| **Common name** | **IUPAC name** | **Function** | **CAS**  **number** | **EC**  **number** | **Content (%)**  **Min/ Max** | |
| --- | --- | --- | --- | --- | --- | --- |
| IR3535® | ethyl 3-[N-acetyl-N-butyl] aminopropionate | Technical active substance | 52304-36-6 | 257-835-0 | 9.75 | 20 |
| Pure active substance | 9.625 | 19.8000 |
| Denatured alcohol (EtOH 50-100% with propan-2-ol 5% and 2-methylpropan-2-ol 0.1%) | Mixture | Solvent | - | - | 20 | 55.53 |

The detailed composition is given in the confidential annex.

**2 .4 Information on technical equivalence**

Not applicable

**2.5 Information on the substance(s) of concern**

Denatured alcohol (EtOH 50-100% with propan-2-ol 5% and 2-methylpropan-2-ol 0.1 %) is a substance of concern for the meta SPC 1 and propan-2-ol contening in this mixture is a substance of concern for the meta SPC 2

**2 .6 Type of formulation**

|  |
| --- |
| AL- Any other liquid  AE - Aerosol dispenser |

**Part II.- Second information level - meta SPC-1**

**1. Meta SPC-1 administrative information**

* 1. **Meta SPC-1 identifier**

| Identifier | Meta SPC-1 Aerosol |
| --- | --- |

**1.2. Suffix to the authorisation number**

|  |  |
| --- | --- |
| Number |  |

**1.3. Product type(s)**

| Product type(s) | PT19 |
| --- | --- |

**2.. Meta SPC-1 composition**

**2.1. Qualitative and quantitative information on the composition of the meta SPC**

The full composition is reported in the confidential annex

| **Common name** | **IUPAC name** | **Function** | **CAS number** | **EC number** | **Content (%)** | |
| --- | --- | --- | --- | --- | --- | --- |
| Min | Max |
| IR3535® | ethyl 3-[N-acetyl-N-butyl] aminopropionate | Pure Active substance | 5230436-6 | 257-835-0 | 9.625 | 9.625 |
| Denatured alcohol (EtOH 50-100% with propan-2-ol 5% and 2-methylpropan-2-ol 0.1%) | Mixture | Solvent | - | - | 55.53 | 55.53 |

**2. 2. Type(s) of formulation of the meta SPC-1**

| Formulation | AE - Aerosol dispenser |
| --- | --- |

**3. Hazard and precautionary statements**

**3. 1 Classification and labelling of the META SPC 1 according to the Regulation (EC) 1272/2008**

| Classification | |
| --- | --- |
| **Hazard category** | Aerosol 1  Eye Irritation 2 |
| **Hazard statement** | H222: Extremely flammable aerosol  H229: Pressurized container: may burst if heated  H319: Causes serious eye irritation |
|  | |
| **Labelling** | |
| **Signal words** | Danger |
| **Hazard statements** | H222: Extremely flammable aerosol  H229: Pressurized container: may burst if heated  H319: Causes serious eye irritation |
| **Precautionary statements** | P102– Keep out of reach of children  P103 –Read label before use  P210 – Keep away from heat/sparks/open flames/hot surfaces. – No smoking.  P211 - Do not spray on an open flame or other ignition source.  P251 – Pressurized container: Do not pierce or burn, even after use.  P264: Wash … thoroughly after handling.  protection/face protection.  P305 + P351 +P338 : IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.  P337 + P313 : If eye irritation persists: Get medical advice/ attention. |
|  | |
| Note |  |

**4. Authorised use(s)**

**4.1 Use description for meta SPC 1**

**Table 1. Use # 1 – Mosquitoes+Phlebotomes / Aerosol / Skin**

|  |  |
| --- | --- |
| Product Type | EU BPR Product type 19: Repellents and attractants (Pest control) |
| Where relevant, an exact description of the authorised use |  |
| Target organism (including development stage) | *Aedes mosquitoes (Aedes spp.)*  *Anopheles mosquitoes (Anopheles spp.)*  *Culex mosquitoes (Culex spp.)*  Sandflies (*Phlebotomus spp*.)  Development stage: adults |
| Field of use | Skin application |
| Application method(s) | Method of application: spraying |
| Application rate(s) and frequency | The application rate is 5.83 g/m²  Protection time: 7 hours.  Adult and child (from 3 years old) : 1 application per day  In France:  Adult and children from 12 years old: 2 applications per day  Child (3-11 years old): 1 application per day or 2 applications per day in areas where there is a risk of zoonosis transmission |
| Category(ies) of users | General public (non-professional) |
| Pack sizes and packaging material | 100 and 150 mL  Aerosol can in aluminium, inner coating with standard epoxy phenolic varnish. |

**4.1.1. Use-specific instructions for use**

|  |
| --- |
| - |

**4.1.2 Use-specific risk mitigation measures**

|  |
| --- |
| - |

**4.1.3 Where specific to the use, the particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment**

|  |
| --- |
| - |

**4.1.4 Where specific to the use, the instructions for safe disposal of the product and its packaging**

|  |
| --- |
| - |

**4.1.5. Where specific to the use, the conditions of storage and shelf-life of the product under normal conditions of storage**

|  |
| --- |
| - |

**5. General directions for useof the meta SPC-1**

**5.1. Instructions for use6**

|  |
| --- |
| * Always read the label or leaflet before use and follow all the instructions provided. * Respect the recommended application doses. * In France - Retreat after water exposure without exceeding the maximal recommended application number (2 applications per day). * The users should report straightforward to the registration holder any alarming signals which could be assumed to be resistance development. * The use of the product with other repellent products is not recommended. * In case of a concomitant use of the product with sunscreen), first apply the sunscreen and wait 20 minutes before the application of the product. * The protection time is only indicative. Environmental factors (e.g. high temperature, wind velocity) can modify it. |

**5.2. Risk mitigation measures**

|  |
| --- |
| * Use only outdoors or in a well-ventilated area. * For adults and children from 3 years old : 1 application per day * Application instructions:   + Adult: 1.2 second/head and/neck, 1.4 second/arm and hand, 2.3 second/leg and foot   + children (6-11 years old): 0.7 second/head and neck, 0.7 second/arm and hand, 1.3 second/leg and foot   + children (3-5 years old) : 0.7 second/head and neck, 0.6 second/arm and hand, 0.8 second/leg and foot   In France :   * 2 applications per day for adults and children from 12 years old. For children (3-11 years old ): 1 applications per day or 2 applications per day in areas where there is a risk of zoonosis transmission * Application instructions   + adult: 1 second/head and neck, 1.4 seconds/arm and hand, and 1.3 seconds/leg ;   + children (6-11 years old): 0.5 second/ head and neck, 0.6 second/¾ arm and 0.6 second/leg ;   + children (3-5 years old) : 0.5 second/ head and neck, 0.3 second/arm, 0.4 second/leg. * Do not use on child below 36 months. * For children between 3 and 11 years old, the product has to be applied by an adult * In France : do not apply on children’s hand * Do not apply directly on the face, spray the product in the hand and then spread it onto the face. * Apply only on area of body without clothes. * Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. Do not pierce or burn, even after use * Avoid any direct or indirect contact with food and feed. |

**5.3. Particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment**

|  |
| --- |
| * Eye contact: Immediately flush with plenty of water, occasionally lifting the upper and lower eyelids. Check for and remove any contact lenses if easy to do. Continue to rinse with warm water for at least 10 minutes. Get medical attention if irritation or vision impairment occurs. * Skin contact: In case of skin lesions, redness or persistent pain after application, consult a doctor. * Inhalation of large quantities: keep at rest in a half-sitting position. Seek medical advice immediately if symptoms occur. * Mouth contact: Wash out mouth with water. Contact poison treatment specialist immediately if symptoms occur and/or in case of mouth contact with large quantities. * Do not give fluids or induce vomiting in case of impaired consciousness; place in recovery position (Left sideways position with the knees bent) and seek medical advice immediately. * Keep the container or label available. * Do not allow product to spread into the environment. * Methods and material for containment and cleaning up: Mechanically ventilate the spillage area. Take up liquid spill into absorbent material, e.g.: sand, saw dust, forward for disposal, clean up affected area. |

**5.4. Instructions for safe disposal of the product and its packaging**

|  |
| --- |
| * Do not discharge unused product on the ground, into water courses, into pipes (sink, toilets…) nor down the drains * Dispose of unused product, its packaging and all other waste in accordance with local regulations. |

**5.5. Conditions of storage and shelf-life of the product under normal conditions of storage**

|  |
| --- |
| * Shelf life : 2 years * Do not expose to temperatures exceeding 40°C and lower than 0°C. |

**6. Other information**

|  |
| --- |
| * Long term tests are ongoing, shelf-life study should be provided whitin two years. * Considering the importance of this active substance in vector control, the authorisation holder has to monitor the resistance phenomenon toward the active substance IR3535. Results of the resistance monitoring must be submitted to the Competent Authorities (CA) or other appointed bodies involved in resistance management every 5 years. * Do not use for pregnant or breast-feeding women. |

**7. Third information level: individual products in the meta SPC-1**

**7.1. Trade name(s), authorisation number and specific composition of each individual product**

| Trade name(s) | Marie Rose Aérosol protection antimoustique | | | | |
| --- | --- | --- | --- | --- | --- |
| Authorisation number |  | | | | |
| Common name | IUPAC name | Function | CAS number | EC number | Content (%) |
| IR3535®, | Ethyl 3-[N-acetyl-N-butyl] aminopropionate | Pure Active substance | 52304-36-6 | 257-835-0 | 9.625 |
| Denatured alcohol (EtOH 50-100% with propan-2-ol 5% and 2-methylpropan-2-ol 0.1%) | Mixture | Solvent | - | - | 55.53 |

**Part II.- Second information level - meta SPC-2**

**1. Meta SPC-2 administrative information**

* 1. **Meta SPC-2 identifier**

| Identifier | Meta SPC-2 Sprays |
| --- | --- |

* 1. **Suffix to the authorisation number**

|  |  |
| --- | --- |
| Number |  |

* 1. **Product type(s**)

| Product type(s) | PT19 |
| --- | --- |

**2. Meta SPC-2 composition**

**2.1. Qualitative and quantitative information on the composition of the meta SPC-2**

The full composition is reported in the confidential annex

| **Common name** | **IUPAC name** | **Function** | **CAS number** | **EC number** | **Content (%)** | |
| --- | --- | --- | --- | --- | --- | --- |
| **Min** | **Max** |
| IR3535® | Ethyl 3-[N-acetyl-N-butyl] aminopropionate | Pure Active substance | 52304-36-6 | 257-835-0 | 19.8 | 19.8 |
| Propan-2-ol |  | Solvent | - | - | 2 | 2 |

**2.2. Type(s) of formulation of the meta SPC-2**

| Formulation | AL- Any other liquid  Liquid formulation, water based |
| --- | --- |

**3. Hazard and precautionary statements of the meta SPC-2**

| **Hazard statements** | H226 - Flammable liquid and vapour  H319 - Causes serious eye irritation |
| --- | --- |
| **Precautionary statements** | P102– Keep out of reach of children  P103 –Read label before use  P210 – Keep away from heat/sparks/open flames/hot surfaces. – No smoking.  P233 - Keep container tightly closed.  P235 - Keep cool  P264: Wash … thoroughly after handling.  P305 + P351 +P338 : IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.  P337 + P313 : If eye irritation persists: Get medical advice/ attention.  P403 – Store in a well-ventilated place.  P403+P235– Store in a well-ventilated place.  P501: Dispose of contents/container in accordance with local/ regional/national/international regulation (to be specified). |

**4. Authorised use(s) of the meta SPC-2**

**4.1. Use description Use # 2 - Mosquitoes+Phlebotomes / Spray / Skin**

**Table 1 Use # 1- Mosquitoes+Phlebotomes / Spray / Skin**

|  |  |
| --- | --- |
| **Corresponding IUCLID Use** | # 2.1 - Mosq/Spray/Adul/Skin  # 2.2 - Mosq/Spray/Chil/Skin |
| **Product Type** | EU BPR Product type 19: Repellents and attractants (Pest control) |
| **Where relevant, an exact description of the authorised use** | - |
| **Target organism (including development stage)** | *Aedes mosquitoes (Aedes spp.)*  *Anopheles mosquitoes (Anopheles spp.)*  *Culex mosquitoes (Culex spp.)*  *Sandflies (Phlebotomus spp.)*  Development stage: adults |
| **Field of use** | Skin application |
| **Application method(s)** | Method of application: spraying |
| **Application rate(s) and frequency** | The application rate is 5.83 g/m².  Protection time: 6.5 hours.  Number and timing of application:  Adult and children from 12 years old: 2 applications per day  Child (3-11years old): 1 application per day  In France:  Adult and children from 12 years old: 2 applications per day  Child (3-11years old): 1 applications per day or 2 applications per day in areas where there is a risk of zoonosis transmission |
| **Category(ies) of users** | General public (non-professional) |
| **Pack sizes and packaging material** | 100 and 150 mL  Airspray in plastic PEHD or PP. |

**4.1.1. Use-specific instructions for use**

|  |
| --- |
| * In France only: Retreat after water exposure without exceeding the maximal recommended application number (2 applications per day). |

**4.1.2 Use-specific risk mitigation measures**

|  |
| --- |
| * Do not apply directly on the face, spray the product on the hand first and spread it on the face. * Application instructions:   + adult: 4-5 stroke/head and neck, 5 stroke/arm and hand, 8 stroke/leg and foot   + children (6 -11 years old)-: 3 stroke/head and neck, 3-4 stroke/arm and hand, 4-5 stroke/leg and foot   + For children (3-6 years old) : 2-3 stroke/head and neck 2 stroke/arm and hand, 3 stroke/leg and foot * In France:   + adult: 4 sprays/head and neck, 4-5 sprays/ arm and hand, 5 sprays/ l legs   + For children (6 -11 years old): 2 sprays/head and neck, 2-3 sprays / arm, and 2-3 sprays/ legs   + children (3-5 years old) : 2 sprays/head and neck, 1 sprays/ arm,,1-2 spray/legs |

**4.1.3 Where specific to the use, the particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment**

|  |
| --- |
| Not specific. |

**4.1.4 Where specific to the use, the instructions for safe disposal of the product and its packaging**

|  |
| --- |
| Not specific. |

**4.1.5. Where specific to the use, the conditions of storage and shelf-life of the product under normal conditions of storage**

|  |
| --- |
| Not specific. |

**4.2. Use description Use# 3- Ticks / Spray / Skin**

**Table 2. Use # 2 - Ticks / Spray / Skin**

|  |  |
| --- | --- |
| **Product Type** | EU BPR Product type 19: Repellents and attractants (Pest control) |
| **Where relevant, an exact description of the authorised use** |  |
| **Target organism (including development stage)** | Ticks (*Ixodes ricinus*)  Development stages: nymphs and adults. |
| **Field of use** | Skin application |
| **Application method(s)** | Method of application: spraying |
| **Application rate(s) and frequency** | The application rate is 7.5 g/m².  Protection time: 6 hours  Number and timing of application:  Adult and Child (from 3 years old): 1 application per day  In France:  Adult and Child (from 3 years old): 1 application per day |
| **Category(ies) of users** | General public (non-professional) |
| **Pack sizes and packaging material** | 100 and 150 mL  Airspray in plastic PEHD or PP |

**4.2.1. Use-specific instructions for use**

|  |
| --- |
| * Not to use for tropical species, demonstrated efficacy for temperate species only. |

**4.2.2 Use-specific risk mitigation measures**

|  |
| --- |
| * Do not apply on the face. * Application instructions:   + adult: 4-5 stroke/head and neck, 5 stroke/arm and hand, 8 stroke/leg and foot   + children (6 -11 years old)-: 3 stroke/head and neck, 3-4 stroke/arm and hand, 4-5 stroke/leg and foot   + For children (3-6 years old) : 2-3 stroke/head and neck 2 stroke/arm and hand, 3 stroke/leg and foot * In France:   + adult: 4 sprays/head and neck, 4-5 sprays/ arm and hand, 5 sprays/ l legs   + For children (6 -11 years old): 2 sprays/head and neck, 2-3 sprays / arm, and 2-3 sprays/ legs   + children (3-5 years old) : 2 sprays/head and neck, 1 spray/ arm,1-2 spray/legs |

**4.2.3 Where specific to the use, the particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment**

|  |
| --- |
| Not specific. |

**4.2.4 Where specific to the use, the instructions for safe disposal of the product and its packaging**

|  |
| --- |
| Not specific. |

**4.2.5. Where specific to the use, the conditions of storage and shelf-life of the product under normal conditions of storage**

|  |
| --- |
| Not specific. |

**5. General directions for useof the meta SPC-2**

**5.1. Instructions for use**

|  |
| --- |
| * Always read the label or leaflet before use and follow all the instructions provided. * Respect the recommended application doses. * The users should report straightforward to the registration holder any alarming signals which could be assumed to be resistance development. * The use of the product with other repellent products is not recommended. * In case of a concomitant use of the product with sunscreen), first apply the sunscreen and wait 20 minutes before the application of the product. * The protection time is only indicative. Environmental factors (e.g. high temperature, wind velocity) can modify it.. |

**5.2. Risk mitigation measures**

|  |
| --- |
| * Do not inhale. * Do not use on child below 36 months. * For children below 11 years old, the product has to be applied by an adult. * Do not apply on child's hand. * Apply only on area of body without clothes * Avoid any direct or indirect contact with food and feed. * Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. * Avoid any direct or indirect contact with food and feed. |

**5.3. Particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment**

|  |
| --- |
| * Eye contact: Immediately flush with plenty of water, occasionally lifting the upper and lower eyelids. Check for and remove any contact lenses if easy to do. Continue to rinse with warm water for at least 10 minutes. Get medical attention if irritation or vision impairment occurs. * Skin contact: In case of skin lesions, redness or persistent pain after application, consult a doctor. * Inhalation: Remove victim to fresh air and keep at rest in a half-sitting position. Seek medical advice immediately if symptoms occur and/or large quantities have been inhaled. * Mouth contact: Wash out mouth with water. Contact poison treatment specialist immediately if symptoms occur and/or in case of mouth contact with large quantities. * Do not give fluids or induce vomiting in case of impaired consciousness; place in recovery position and seek medical advice immediately. * Keep the container or label available. * Symptomatic treatment, no antidote available. * Do not allow product to spread into the environment. * Methods and material for containment and cleaning up: Mechanically ventilate the spillage area. Take up liquid spill into absorbent material, e.g.: sand, saw dust, forward for disposal, clean up affected area. |

**5.4. Instructions for safe disposal of the product and its packaging**

|  |
| --- |
| * Do not discharge unused product on the ground, into water courses, into pipes (sink, toilets…) nor down the drains * Dispose of unused product, its packaging and all other waste in accordance with local regulations. |

**5.5. Conditions of storage and shelf-life of the product under normal conditions of storage**

|  |
| --- |
| * Shelf life : 2 years * Do not expose to temperatures exceeding 40°C and lower than 0°C. |

**6. Other information**

|  |
| --- |
| * Considering the importance of this active substance in vector control, the authorisation holder has to monitor the resistance phenomenon toward the active substance IR3535. Results of the resistance monitoring must be submitted to the Competent Authorities (CA) or other appointed bodies involved in resistance management every 5 years. * Do not use for pregnant or breast-feeding women * The number of sprays indicated on the label should be adapted to the application rate. * Final shelf-life study should be provided within two years |

**7. Third information level: individual products in the meta SPC-2**

**7.1. Trade name(s), authorisation number and specific composition of each individual product**

| **Trade name(s)** | Marie Rose Répulsif anti-moustiques  Marie Rose Répulsif anti-tiques  Marie Rose Spray corporel répulsif anti-moustiques  Marie Rose spray répulsif et apaisant anti-moustiques  Marie Rose spray corporel 2 en 1 anti-moustiques | | | | |
| --- | --- | --- | --- | --- | --- |
| **Authorisation number** |  | | | | |
| **Common name** | **IUPAC name** | **Function** | **CAS number** | **EC number** | **Content (%)** |
| **IR3535®** | Ethyl 3-[N-acetyl-N-butyl] aminopropionate | Active substance | 5230436-6 | 257-835-0 | 19.8 |
| Propan-2-ol |  | Solvent | - | - | 2 |

## Packaging of the biocidal product

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Type of packaging** | **Size/volume of the packaging** | **Material of the packaging** | **Type and material of closure(s)** | **Intended user (e.g. professional, non-professional)** | **Compatibility of the product with the proposed packaging materials (Yes/No)** |
| Bottle | 100 mL | Aluminium inner coating with standard epoxy phenolic vamish  Nozzle and valve. Push-button in polypropylene. |  | Non-professional |  |
| Bottle | 150 mL | Aluminium inner coating with standard epoxy phenolic vamish  Nozzle and valve. Push-button in polypropylene. |  | Non-professional |  |
| Bottle | 100 mL | HDPE or PP |  | Non-professional |  |
| Bottle | 150 mL | HDPE or PP |  | Non-professional |  |

## Documentation

### Data submitted in relation to product application

Physico-chemical properties studies and analytical methods on the biocidal product Famille Juva Repulsif Insectes were provided by JUVA SANTE.

The following studies have been submitted for the efficacy:

* An arm-in-cage study conducted with ten human volunteers with the product Marie rose aerosol protection anti-moustiques référence 096560 (14% w/w IR3535) applied on skin with four mosquito species (*Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens*).
* An arm-in-cage study conducted with ten human volunteers with the product Marie rose aerosol protection anti-moustiques référence 096560 (13.8% w/w IR3535) applied on skin with two mosquito species (*Anopheles gambiae, Aedes albopictus*) and one sand fly species (*Phlebotomus duboscqi*).
* An arm-in-cage study conducted with ten human volunteers with the product Marie rose spray protection anti-moustiques référence 096602 (20% w/w IR3535) applied on skin with four mosquito species (*Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens*) and one sand fly species (*Phlebotomus duboscqi*).
* A laboratory study conducted with ten mice with the product Marie rose spray protection anti-moustiques référence 096602 (20% w/w IR3535) with one tick species (*Ixodes ricinus*).

### Active Substance

Please refer to Annex 3.3 for a list of additional studies, supplied by the Active Substance data holder, not contained within IR3535 Assessment Report.

#### Access to documentation

The applicant is the data holder of the product data and has been submitted a letter of Access from Merck KGaA/Merck S.L.U to the active substance data.

## Assessment of the biocidal product (family)

### Intended use(s) as applied for by the applicant

Table 2. Use # 1 – Mosquitoes+Phlebotomes / Aerosol / Skin

|  |  |
| --- | --- |
| **Product Type** | EU BPR Product type 19: Repellents and attractants (Pest control) |
| **Where relevant, an exact description of the authorised use** | The biocidal product can be applied directly to skin. The product can be used on a daily basis during the period of infestation/contact and exposure to the targets (seasonal/daily period of activity).  Application of the biocidal product must be done by adults only, at around 10 cm from skin and outdoor or in well aerated room.  For direct application to skin, the product can be applied twice a day on face, legs, arms and hands for adults and on face, legs and arms for children. The treatment of child’s hands is not recommended. Do not apply directly on the face, spray the product on the hand first and spread it on the face.  Protection period of 7h per application. |
| **Target organism (including development stage)** | Scientific name: Culicidae, common name: *Aedes* mosquitoes (*Aedes* sp. (*A. aegypti*, *A. albopictus*)), development stage: adults  Scientific name: Culicidae, common name: *Anopheles* mosquitoes (*Anopheles* sp. (*A. gambiae*)), development stage: adults  Scientific name: Culicidae, common name: mosquitoes (*Culex* sp. (*C. pipiens*)), development stage: adults  Scientific name: Psychodidae, common name: sandflies (*Phlebotomus* sp. (*P. duboscqi*)), development stage: adults |
| **Field of use** | indoor use  outdoor use |
| **Application method(s)** | **Method of application:** spraying  **Detailed description of the method:**  Spraying on skin at 10 cm on face, arms, legs, hands for adult and face, arms, legs for child (>3years) |
| **Application rate(s) and frequency** | **The application rate is** ca. 5.83 g/m² **for the dilution** 9.75 %**.**  **Number and timing of application:** Adult: 2 applications per day  Child>3years: 2 applications per day  Application instructions :  Adult: per arm 1 seconde/per leg 4 sec/face 1 sec  Child: per arm <1 seconde/per leg 1-2 sec/face <1 sec |
| **Category(ies) of users** | General public (non-professional) |
| **Pack sizes and packaging material** | 100 and 150 mL  Aerosol can in aluminium, inner coating with standard epoxy phenolic varnish.  Please see the relevant section. |

Table 3. Use # 2 – Mosquitoes+Phlebotomes / Spray / Skin

|  |  |
| --- | --- |
| **Product Type** | EU BPR Product type 19: Repellents and attractants (Pest control) |
| **Where relevant, an exact description of the authorised use** | The biocidal product can be applied directly to skin. The product can be used on a daily basis during the period of infestation/contact and exposure to the targets (seasonal/daily period of activity).  Application of the biocidal product must be done by adults only, at around 10 cm from skin and outdoor or in well aerated room.  For direct application to skin, the product can be applied on face, legs, arms and hands for adults and on face, legs and arms for children. The number of application per day is limited to one for children (>3 years) and two for adults. The treatment of child’s hands is not recommended. Do not apply directly on the face, spray the product on the hand first and spread it on the face.  Protection period of 7h per application. |
| **Target organism (including development stage)** | Scientific name: Culicidae, common name: *Aedes* mosquitoes (*Aedes* sp. (*A. aegypti, A. albopictus*)), development stage: adults  Scientific name: Culicidae, common name: *Anopheles* mosquitoes (*Anopheles* sp. (*A. gambiae*)), development stage: adults  Scientific name: Culicidae, common name: mosquitoes (*Culex* sp. (*C. pipiens*)), development stage: adults  Scientific name: Psychodidae, common name: sandflies (*Phlebotomus* sp. (*P. duboscqi*)), development stage: adults |
| **Field of use** | outdoor use  indoor use |
| **Application method(s)** | **Method of application:** spraying  **Detailed description of the method:**  Spraying on skin at 10 cm on face, arms, legs, hands for adult and face, arms, legs for child (>3years) |
| **Application rate(s) and frequency** | **The application rate is** ca. 5.83 g/m² **for the dilution** 20%**.**  **Number and timing of application:** Adult: 2 applications per day  Child>3years: 1 application per day  Application instructions :  Adult: per arm 4 sprays/per leg 9 sprays/face 1 spray  Child: per arm 2 sprays/per leg 3 sprays/face 1 spray |
| **Category(ies) of users** | General public (non-professional) |
| **Pack sizes and packaging material** | 100 and 150 mL  Airspray in plastic PEHD or PP.  Please see the relevant section. |

Table 4. Use # 3 – Ticks / Spray / Skin

|  |  |
| --- | --- |
| **Product Type** | EU BPR Product type 19: Repellents and attractants (Pest control) |
| **Where relevant, an exact description of the authorised use** | The biocidal product can be applied directly to skin. The product can be used on a daily basis during the period of infestation/contact and exposure to the targets (seasonal/daily period of activity).  Application of the biocidal product must be done by adults only, at around 10 cm from the skin and outdoor or in well aerated.  For direct application to skin, the product can be applied on the neck, legs and arms, once a day for adults and children (> 3 years). The treatment of child’s hands is not recommended. Do not apply on the face.  Protection period of 6h per application. |
| **Target organism (including development stage)** | Scientific name: Ixodidae, common name: ticks (*Ixodes ricinus*), development stage: Nymphs and adults. |
| **Field of use** | outdoor use |
| **Application method(s)** | **Method of application:** spraying  **Detailed description of the method:**  Spraying on skin at 10 cm on neck, legs and arms for adult and child (>3years). |
| **Application rate(s) and frequency** | **The application rate is** ca. 7.5 g/m² **for the dilution** 20%**.**  **Number and timing of application:**  Adult: 1 application per day  Child>3years: 1 application per day  Application instructions :  Adult: per arm 5 sprays/per leg 11 sprays/neck 2 sprays  Child: per arm 2 sprays/per leg 4 sprays/neck 1 spray |
| **Category(ies) of users** | General public (non-professional) |
| **Pack sizes and packaging material** | 100 and 150 mL  Airspray in plastic PEHD or PP.  Please see the relevant section. |

Table 5. Use # 4 – Mosquitoes+Phlebotomes+Ticks / Spray / Skin

|  |  |
| --- | --- |
| **Product Type** | EU BPR Product type 19: Repellents and attractants (Pest control) |
| **Where relevant, an exact description of the authorised use** | The biocidal product can be applied directly to skin. The product can be used on a daily basis during the period of infestation/contact and exposure to the targets (seasonal/daily period of activity).  Application of the biocidal product must be done by adults only, at around 10 cm from skin and outdoor or in well aerated room.  For direct application to skin, the product can be applied on face, neck, legs, arms and hands for adults and on face, neck, legs and arms for children. The number of application per day is limited to one for adults and children (>3 years). The treatment of child’s hands is not recommended. Do not apply directly on the face, spray the product on the hand first and spread it on the face.  Protection period of 6.5h per application for mosquitoes and phlebotomes and 6h per application for ticks. |
| **Target organism (including development stage)** | Scientific name: Culicidae, common name: *Aedes* mosquitoes (*Aedes* sp. (*A. aegypti, A. albopictus*)), development stage: adults  Scientific name: Culicidae, common name: *Anopheles* mosquitoes (*Anopheles* sp. (*A. gambiae*)), development stage: adults  Scientific name: Culicidae, common name: mosquitoes (*Culex* sp. (*C. pipiens*)), development stage: adults  Scientific name: Psychodidae, common name: sandflies (*Phlebotomus* sp. (*P. duboscqi*)), development stage: adults  Scientific name: Ixodidae, common name: ticks (*Ixodes ricinus*), development stage: Nymphs and adults. |
| **Field of use** | outdoor use  indoor use |
| **Application method(s)** | **Method of application:** spraying **Detailed description of the method:**  Spraying on skin at 10 cm on face, neck, legs, arms and hands for adult and on face, neck, legs and arms for child (>3years). |
| **Application rate(s) and frequency** | **The application rate is** ca. 7.5 g/m² **for the dilution** 20 %**.**  **Number and timing of application:**  Adult: 1 application per day  Child>3years: 1 application per day  Application instructions :  Adult: per arm 5 sprays/per leg 11 sprays/neck 2 sprays/face 2 sprays/ hands 3 sprays  Child: per arm 2 sprays/per leg 4 sprays/neck 1 spray/face 1 spray |
| **Category(ies) of users** | General public (non-professional) |
| **Pack sizes and packaging material** | 100 and 150 mL  Airspray in plastic PEHD or PP.  Please see the relevant section. |

### Physical, chemical and technical properties

The biocidal products are not the same as the one assessed for the inclusion of the active substances in annex 1 of directive 98/8/EC. The composition of the products are confidential and are presented in a confidential annex. The products contain 9.75-20 % of technical active substance IR3535 and 9.65-19.8% of pure active substance IR3535 (purity 99 %).

The products do not contain PT6 preservative. There is no compound classified H304 > 10 %.

The physico-chemical properties tested for meta SPC 1 are performed on the degased product.

The product is ready-to-use.

Formulation type: Meta SPC 1 : AE (Aerosol)

meta SPC 2 : AL (All other Liquid)

The complete results are summerised below:

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **FR Evaluation** | **Reference** |
| --- | --- | --- | --- | --- | --- |
| Physical state at 20 °C and 101.3 kPa | CIPAC MT 46.3 + visual inspection  GLP | Product 096560: META SPC 1 batches 01 and 02 packaging grey aluminium spray degased product  Product 096587: META SPC 2b batch: LJP15-167 packaging white HDPE spray | |  |  |  | | --- | --- | --- | |  | Appearance | packaging | | Meta SPC 1 | Homogeneous colourless limpid liquid | Grey opaque aluminium spray | | Meta SPC 2 | Homogeneous colourless limpid liquid | White opaque HDPE spray | | Acceptable | Anonymous (2015), study number 15-912036-004  Anonymous  (2015), study number 15-912036-009 |
| Colour at 20 °C and 101.3 kPa | CIPAC MT 46.3 + visual inspection  GLP | Product 096560: META SPC 1 batches 01 and 02 packaging grey aluminium spray degased product  Product 096587: META SPC 2b batch: LJP15-167 packaging white HDPE spray | |  |  |  | | --- | --- | --- | |  | Appearance | packaging | | Meta SPC 1 | Homogeneous colourless limpid liquid | Grey opaque aluminium spray | | Meta SPC 2 | Homogeneous colourless limpid liquid | White opaque HDPE spray | | Acceptable | Anonymous (2015), study number 15-912036-004  Anonymous  (2015), study number 15-912036-009 |
| Odour at 20 °C and 101.3 kPa | CIPAC MT 46.3 + visual inspection  GLP | Product 096560: META SPC 1 batches 01 and 02 packaging grey aluminium spray degased product  Product 096587: META SPC 2b batch: LJP15-167 packaging white HDPE spray | |  |  |  | | --- | --- | --- | |  | Appearance | packaging | | Meta SPC 1 | Homogeneous colourless limpid liquid | Grey opaque aluminium spray | | Meta SPC 2 | Homogeneous colourless limpid liquid | White opaque HDPE spray | | Acceptable | Anonymous (2015), study number 15-912036-004  Anonymous  (2015), study number 15-912036-009 |
| Acidity / alkalinity | CIPAC MT 75.3  CIPAC MT 46.3  GLP | Product 096560: META SPC 1 batches 01 and 02 packaging grey aluminium spray 15%w/w IR3535 degased product  Product 096587: META SPC 2b batch: LJP15-167 packaging white HDPE spray 20.4%w/w IR3535 | |  |  |  | | --- | --- | --- | |  | pH pure | After storage pH pure | | Meta SPC 1 | 5.48 at 20.3°C | 4.39 at 20.6°C | | Meta SPC 2 | 5.82 at 21°C | 5.8 at 21.6°C | | Acceptable | Anonymous (2015), study number 15-912036-004  Anonymous  (2015), study number 15-912036-009 |
| Relative density / bulk density | EC A3 Method OECD N° 109 (2012)  GLP | Product 096560: META SPC 1 batches 01 and 02 packaging grey aluminium spray 15%w/w IR3535 degased product  Product 096587: META SPC 2b batch: LJP15-167 packaging white HDPE spray 20.4%w/w IR3535 | |  |  | | --- | --- | |  | Relative density | | Meta SPC 1 | 0.817 at 21.3°C | | Meta SPC 2 | 0.976 at 19.4°C | | Acceptable | Anonymous (2015), study number 15-912036-003  Anonymous  (2015), study number 15-912036-008 |
| Storage stability test – **accelerated storage** | *Method MT46.3*  Method to quantify the AS study n° 15-912036-006  GLP | Product 096560: META SPC 1 batches 01 and 02 packaging grey aluminium spray 15%w/w IR3535 degased product  Product 096587: META SPC 2b batch: LJP15-167 packaging white HDPE spray 20.4%w/w IR3535  Packaging HDPE spray | *After 8 weeks at 40°C*  Type of formulation : AL :META SPC 2   |  |  |  | | --- | --- | --- | |  | T0 | T8weeks at 40°C | | Appearance | Homogeneous colourless limpid liquid | No change | | Appearance of packaging | White opaque HDPE spray | No change | | AS content | 20.4 % w/w | 20.1% w/w | | % variation | / | -1.5 % | | pH | 5.48 at 20.3°C | 4.39 at 20.6°C | | Determination of the satisfactory operation of the spray | No blocking pump  Pump and trigger ok | No change | | Spray volume | 0.17 mL | 0.18 mL |   Type of formulation : AE :META SPC 1   |  |  |  | | --- | --- | --- | |  | T0 | T8weeks at 40°C | | Appearance | Homogeneous colourless limpid liquid | No change | | Appearance of packaging | Grey opaque aluminium spray | No change | | AS content | 15 % w/w | 14.9 % w/w | | % variation | / | -0.7 % | | pH | 5.82 at 21°C | 5.80 at 21.6°C | | Determination of the satisfactory operation of the aerosol | The nozzle of the aerosol was checked: no blocking | No change | | Spray weight (one pulverization during 5”) | 3.1 g | 3.0 g | | Spray diameter and pattern | The shape of the spray is circular.  Mean spray diameter is 8 cm | No change  Mean spray diameter is 6 cm | | Acceptable  Products of the META SPC 1 and META SPC 2 are stable 8 weeks at 40°C in bottles in HDPE or in bottles in aluminum. The products should not be store at a temperature > 40°C. | Anonymous (2015), study number 15-912036-004  Anonymous  (2015), study number 15-912036-009 |
| Storage stability test – **long term storage at ambient temperature** | - | - | Studies are on-going. | The studies of long term storage should be provided at the post-authorisation stage.  **Post authorisation data – FAMILLE JUVA REPULSIF INSECTES – 2021 :**  Long term storage studies have been provided. Please refer to the table below. | *-* |
| Storage stability test – **low temperature stability test for liquids** | - | - | The low temperature storage does not need to be addressed since the label gives clear instructions that the product must not be stored under conditions of ≤ 0°C. | Acceptable | IUCLID |
| Effects on content of the active substance and technical characteristics of the biocidal product - **light** | - | - | Considering the opaque to light packaging of all the biocidal products, the effect of light has not been determined. The AS is photolytically stable. | Acceptable | IUCLID |
| Effects on content of the active substance and technical characteristics of the biocidal product – **temperature and humidity** | - | - | *-* | Data on temperature have been provided in the accelerated storage stability study. | *-* |
| Effects on content of the active substance and technical characteristics of the biocidal product - **reactivity towards container material** | - | - | Cf: storage stability studies. | Bottles of 100-150 mL in HDPE with a pump in PP or HDPE are acceptable for META SPC 2 and bottles of 100-150 mL in aluminium with nozzle are acceptable. | - |
| Wettability | - | - | Not applicable | Not relevant for an AL and AE formulation | *-* |
| Suspensibility, spontaneity and dispersion stability | - | - | Not applicable | Not relevant for an AL and AE formulation | *-* |
| Wet sieve analysis and dry sieve test | - | - | Not applicable | Not relevant for an AL and AE formulation | *-* |
| Emulsifiability, re-emulsifiability and emulsion stability | - | - | Not applicable | Not relevant for an AL and AE formulation, there are ready-to-use. | *-* |
| Disintegration time | - | - | Not applicable | Not relevant for an AL and AE formulation | *-* |
| Particle size distribution, content of dust/fines, attrition, friability | - | - | Not applicable | Not relevant for an AL and AE formulation, there are ready-to-use. | *-* |
| Persistent foaming | - | - | Not applicable | Not relevant for an AL and AE formulation, there are ready-to-use. | *-* |
| Flowability/Pourability/Dustability | - | - | Not applicable | Not relevant for an AL and AE formulation, there are ready-to-use. | *-* |
| Burning rate — smoke generators | - | - | Not applicable | Not relevant for an AL and AE formulation | *-* |
| Burning completeness — smoke generators | - | - | Not applicable | Not relevant for an AL and AE formulation | *-* |
| Composition of smoke — smoke generators | - | - | Not applicable | Not relevant for an AL and AE formulation | *-* |
| Spraying pattern — aerosols | Internal method equivalent to the FEA 644 method  GLP | Product 096587: META SPC 2b batch: LJP15-167 packaging white HDPE spray 20.4% w/w IR3535 | Product 096587: The mean spray diameter of a multi-shot aerosol was 8 cm.  The shape of the spray on the wetted patch was circular. | Acceptable | Anonymous (2015), study number 15-912036-004  Anonymous  (2015), study number 15-912036-009 |
| Physical compatibility | Statement | - | No other substances, mixtures, biocidal or non-biocidal products are to be co-applied with the biocidal products. | Not relevant for a ready-to-use | IUCLID |
| Chemical compatibility | Statement | - | No other substances, mixtures, biocidal or non-biocidal products are to be co-applied with the biocidal products. | Not relevant for a ready-to-use | IUCLID |
| Degree of dissolution and dilution stability | - | - | Not applicable | Not relevant for an AL and AE formulation | *-* |
| Surface tension | EC A5 Method OECD N° 115(1995)  GLP | Product 096560: META SPC 1 batches 01 and 02 packaging grey aluminium spray 15%w/w IR3535 degased product  Product 096587: META SPC 2b batch: LJP15-167 packaging white HDPE spray 20.4%w/w IR3535 | |  |  | | --- | --- | |  | Surface tension | | Meta SPC 1 | 22.4 mN/m at 20.3°C | | Meta SPC 2 | 30.4mN/m at 20.1°C | | Acceptable | Anonymous (2015), study number 15-912036-003  Anonymous  (2015), study number 15-912036-008 |
| Viscosity | OECD N° 114 (2012) ISO Std 3219  GLP | Product 096560: META SPC 1 batches 01 and 02 packaging grey aluminium spray 15%w/w IR3535 degased product  Product 096587: META SPC 2b batch: LJP15-167 packaging white HDPE spray 20.4%w/w IR3535 | |  |  | | --- | --- | |  | Relative density | | Meta SPC 1 | 3.98 mPa.s at 20°C  2.19 mPa.s at 40°C | | Meta SPC 2 | 1.5 mPa.s at 20°C 1.07 mPa.s at 40°C | | Acceptable | Anonymous (2015), study number 15-912036-003  Anonymous  (2015), study number 15-912036-008 |
| Droplet size | No guideline available | Product 096560: META SPC 1 batches 01 and 02 packaging grey aluminium spray degased product  Product 0966602: META SPC 2b batch: FLAC 0625(PP) + FLAC0683 5HDPE) | |  |  |  |  | | --- | --- | --- | --- | |  | Droplet size (Dv50) | Inhalable proportion (<10 µm) | Respirable fraction (<50µm) | | Meta SPC 1 | 50.3 µm | <10% (mean 2,17%) | Mean: 45% | | Meta SPC 2 (PP) | 79 µm | <10%(mean 0,58%) | Mean 18% | | Meta SPC 2 (HDPE) | 76µm | <10%(mean 0,69%) | Mean 20% | | Acceptable | Preterre D. 2018,  report G51-20150717 |

* **Post authorisation data – FAMILLE JUVA REPULSIF INSECTES – 2021 :**

Long term storage stability study:

|  |  |  |  |
| --- | --- | --- | --- |
| Guideline and method | Results | Reference | Comment |
| Technical monograph N°.17  For AS content GC-FID  was followed (method already validated in study 15-912036-006)  pH determination  CIPAC MT 75.3 | Product of Meta spc 2  Temperature : 20°C ± 2°C   |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | | months | T0 | T3 | T6 | T12 | T18 | T24 | T36 | | Appearance of test item | Homogeneous colourless limpid liquid | No change | No change | No change | No change | No change | No change | | Appearance of the packaging (HDPE) | White opaque PP crimped spray | No change | No change | No change | No change | No change | No change | | Appearance of the packaging (PP) | White opaque PP crimped spray | No change | No change | No change | No change | No change | No change | | Weight loss % (PP packaging) | - | -0.1 | -0.2 | -0.2 | -0.2 | -0.3 | -0.4 | | Weight loss % (HDPE packaging) | - | 0 | -0.1 | -0.1 | -0.2 | -0.2 | -0.4 | | Content of AS Ethyl butylacetylaminopropionate in PP %w/w  (% of variation) | 20.1% | 20.3%  (+1%) | 20.1%  (0 %) | 20.0%  (-0.5%) | 19.7%  (-2%) | 19.4%  (-3.5%) | 19.3%  (-4%) | | Content of AS Ethyl butylacetylaminopropionate in HDPE %w/w  (% of variation) | 20.1% | 20.2%  (+0.5%) | 20.3%  (-0.5%) | 20.0%  (-0.5%) | 20.0%  (-0.5%) | 19.3%  (-4%) | 18.8%  (-6.5%) | | Spray volume for PP packaging | 0.18 mL  Nozzles checked, no blocking | - | - | - | - | 0.18 mL  Nozzles checked, no blocking | 0.18 mL  Nozzles checked, no blocking | | Spray volume for HDPE packaging | 0.18 mL  Nozzles checked, no blocking | - | - | - | - | 0.18 mL  Nozzles checked, no blocking | 0.19 mL  Nozzles checked, no blocking | | pH (PP packaging) | 6.32  (at 21.5 °C) | - | - | - | - | 3.72  (at 20 °C) | 3.32  (at 21 °C) | | pH (HDPE packaging) | 6.28  (at 20.9°C) | - | - | - | - | 3.72  (at 20.1°C) | 3.34  (at 20.9°C) | | Report No. 17-912036-001  C. Loufrani, 2020 | Acceptable.  Product of the META SPC2 is stable in PP and HDPE packaging for 36 months at 20°C.  A justification was submitted by the applicant concerning pH variations during the test.  The decrease of pH over time (after 24 and 36 months) is related to the transformation of the active substance in its free-acid form.  pH variation is accompanied with a variation in the content of AS (-4% in PP and -6.5% in HDPE).  The product tested during the long term storage study (META SPC2b) contains a buffer at 0.009%.  Given the results obtained with META SPC 2b (buffer at 0.009%); greater degradation of the AS may occur for products without buffer (0%).  Thus the range of the buffer was changed to 0.009-0.1%. |
| Technical monograph N°.17  For AS content, GC-FID method already validated in study N° 15-912036-011  pH determination  CIPAC MT 75.3 | Product of meta spc 1  Temperature : 30°C ± 2°C   |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | |  | Before storage | After 12 months | After 24 months | After 30 months | After 36 months | | Appearance of test item | Homogeneous colourless limpid liquid | | | | | | Appearance of the packaging (aluminium) | Grey opaque aluminium spray (no sign of degradation or leak) | | | | | | Content of AS Ethyl butylacetylaminopropionate in aluminium %w/w  (% of variation) | 15% | 15.7%  (+4.7%) | 15.5%  (+3.3%) | 15.6%  (+4%) | 15.2%  (+1.3%) | | Determination of the satisfactory operation of the aerosol | The nozzle of the aerosol was checked and no blocking was observed | - | No change | - | No change | | Spray weight (one pulverization during 5”) (g) | 3.1 | - | 3.2 | - | 3.1 | | Spray diameter and pattern | Circular shape  8cm | - | Circular shape 12 cm | - | Circular shape 13 cm | | pH | 5.82 (at 21 °C) | - | 5.99 (at 21.9°C) | - | 6.71 (at 19.4°C) | | Report No. 15-912036-010  Marie-Laure Teisseire, 2019 | Acceptable.    Product of the META SCP1 is stable in aluminium packaging for 36 months at 30°C.. |

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| **FR CA Conclusion on the physical, chemical and technical properties of the product** |
| The product of the meta SPC 1 is an aerosol (AE) formulation. All studies have been performed in accordance with the current requirements and the results are deemed to be acceptable.  The appearance of the product is an homogeneous limpid liquid colourless. There is no effect of high temperature on the stability of the formulation, since after 8 weeks at 40°C, neither the active ingredient content nor the technical properties were changed. The stability data indicate a shelf life of at least 2 years at ambient temperature (do not expose to temperatures exceeding 40°C and lower than 0°C) when stored in aluminium bottle packaging material (commercial packaging material). The long term storage stability study (36 months) is on-going.  Its technical characteristics are acceptable for an AE formulation.  Products of meta SPC 2 are all other liquids formulation. All studies have been performed in accordance with the current requirements and the results are deemed to be acceptable.  The appearance of the product is an homogeneous limpid liquid colourless. There is no effect of high temperature on the stability of the formulation, since after 8 weeks at 40°C, neither the active ingredient content nor the technical properties were changed. The stability data indicate a shelf life of at least 2 years at ambient temperature (do not expose to temperatures exceeding 40°C and lower than 0°C) when stored in HDPE bottle packaging material (commercial packaging material). The long term storage stability study (36 months) is on-going.  Its technical characteristics are acceptable for an AL formulation.  **Data required in post-authorisation**  The studies of long term storage should be provided in post authorisation.   * **Post authorisation data – FAMILLE JUVA REPULSIF INSECTES – 2021** :   Long term storage study shows that META SPC1 product remains stable after 3 years at 30°C in aluminium packaging.  Long term storage study shows that META SPC2 product remains stable after 3 years at 20°C in HDPE or PP packaging.  However, a decrease of pH over time (after 24 and 36 months) was observed. It is related to the transformation of the active substance in its free-acid form.  Restriction in the composition has been applied, please refer to confidential annex for further details.  A shelf-life of 2 years is currently authorized and confirmed. A minor change application should be submitted in order to claim a shelf-life of 3 years . |

### Physical hazards and respective characteristics

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **FR evaluation** | **Reference** |
| --- | --- | --- | --- | --- | --- |
| Explosives | Internal method +EC A14  GLP | Product 096560: META SPC 1 batches 01 and 02 packaging grey aluminium spray 15%w/w IR3535 degased product  Product 096587: META SPC 2b batch: LJP15-167 packaging white HDPE spray 20.4%w/w IR3535 | |  |  | | --- | --- | |  | Explosive properties | | Meta SPC 1 | No exothermic reaction, not explosive. | | Meta SPC 2 | No exothermic reaction, not explosive. | | Acceptable  The biocidal products have no explosive properties. | Anonymous (2015), study number 15-912036-003  Anonymous  (2015), study number 15-912036-008 |
| Flammable gases | - | - | Not applicable | Not relevant as the products are a liquid and an aerosol | - |
| Flammable aerosols | EC N)440/2008, EC A9, ISO Std 3679  GLP | Product 096560: META SPC 1 batches 01 and 02 packaging grey aluminium spray 15%w/w IR3535 degased product | Flash point: 15°C | Acceptable, the product is extremely flammable, the product is classified cat. 1 H222 | Anonymous  (2015), study number 15-912036-008 |
| Oxidising gases | - | - | Not applicable | Not relevant as the products are a liquid and an aerosol | - |
| Gases under pressure | - | - | Not applicable | Not relevant as the products are a liquid and an aerosol | - |
| Flammable liquids | EC N°440/2008, EC A9, ISO Std 3679  GLP | Product 096587: META SPC 2b batch: LJP15-167 packaging white HDPE spray 20.4%w/w IR3535 | Flash point: 37°C | Acceptable  The product is flammable liquid and vapour, the product is classified Cat.3 H226 | Anonymous (2015), study number 15-912036-003 |
| Flammable solids | - | - | Not applicable | Not relevant as the products are a liquid and an aerosol | - |
| Self-reactive substances and mixtures | Statement | - | According to the UN Manual of Tests and Criteria, 5th revised Edition (2010), the classification procedure for self-reactive substances (section 20.4) need not to be applied if the exothermic decomposition energy is less than 300 J/g. The onset temperature and decomposition energy were estimated using a Differential Scanning Calorimetry and no exothermic reaction was observed. | Acceptable | IUCLID |
| Pyrophoric liquids | Statement | - | Experience in manufacture or handling shows that the liquid does not ignite spontaneously on coming into contact with air at normal temperatures (i.e. the liquid is known to be stable at room temperature for prolonged periods of time (days)). | Acceptable | IUCLID |
| Pyrophoric solids | - | - | Not applicable | Not relevant as the products are a liquid and an aerosol | - |
| Self-heating substances and mixtures | Statement | - | In general, the phenomenon of self-heating applies only to solids. The surface of liquids is not large enough for reaction with air and the test method is not applicable to liquids. Therefore liquids are not classified as self-heating. However, if liquids are adsorbed on a large surface (e.g. on powder particles), a self-heating hazard should be considered. This is not the case for the considered biocidal products. | Acceptable | IUCLID |
| Substances and mixtures which in contact with water emit flammable gases | Statement | - | This determination is not required since:  1- The chemical structure of the substances constituting the biocidal products do not contain metals or metalloids  2- Experience in handling and use shows that the substances and the products do not react with water (the substance contains water) | Acceptable | IUCLID |
| Oxidising liquids | Statement | - | This determination is not to be required since:  (a) The constituents of the biocidal products do not contain any fluorine or chlorine; but only oxygen but:  (b) The constituents of the biocidal products contain oxygen, but this element is always chemically bonded only to carbon or hydrogen. | Acceptable | IUCLID |
| Oxidising solids | - | - | Not applicable. | Not relevant as the product is not a solid |  |
| Organic peroxides | Statement | - | Organic peroxides are classified by definition based on their chemical structure and on the available oxygen and hydrogen peroxide content of formulations. None of the formulations contain peroxide structures. | Acceptable | IUCLID |
| Corrosive to metals | Manuel d’épreuves et de critères des Nation Unies” part 37  GLP | Product 096587: META SPC 2b  Aluminium alloy and steel  Product 096560  Aluminium alloy and steel | Following the 168 hours of test of Marie-Rose Spray 2 en 1 Ref 096587 product with both carbon steel and aluminium alloy specimens, a weight loss lower than 13.5% was obtained and a maximum depth of attack lower than 120 µm was measured: the corrosiveness of the product Marie-Rose Spray Ref 096587 is not grade 8.  Following the 168 hours of test of Marie-Rose Aerosol Ref 096560 product with both carbon steel and aluminium alloy specimens, a weight loss lower than 13.5% was obtained and a maximum depth of attack lower than 120 µm was measured: the corrosiveness of the product Marie-Rose aerosol Ref 096560 is not grade 8. | Acceptable | Chambouvet L. (2015), Report PV/239/15/LC  Chambouvet L. (2015), Report PV/249/15/LC |
| Auto-ignition temperatures of products (liquids and gases) | EC n°440/2008  EC A15 method  GLP | Product 096560: META SPC 1 batches 01 and 02 packaging grey aluminium spray 15%w/w IR3535 degased product  Product 096587: META SPC 2b batch: LJP15-167 packaging white HDPE spray 20.4%w/w IR3535 | Product 096587 : 450°C  Product 096560: 397°C | Acceptable  The products are not auto-flammable at ambient temperature. | Anonymous (2015), study number 15-912036-003  Anonymous  (2015), study number 15-912036-008 |
| Relative self-ignition temperature for solids | - | - | Not applicable. | Not relevant as the product is not a solid. | - |
| Dust explosion hazard | - | - | Not applicable. | Not relevant as the product is a liquid and an aerosol. | - |

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| **FR CA Conclusion on the physical hazards and respective characteristics of the product** |
| The products in the META SPC 1 are classified extremely flammable aerosol cat.1 H222.  The products in the META SPC 2 are classified flammable liquid and vapour cat.3 H226. |

### Methods for detection and identification

META SPC 1: product reference 096560

Report: Anonymous 2015

Report no 15-912036-011

Test facility:

DEFITRACES

Z.A. des Andrés

150, rue Pré-Magne

69126 BRINDAS

FRANCE

Principle of the method:

Ethyl butylacetylaminopropionate (IR3535) is analysed after extraction from the formulation and quantified by gas chromatography with a FID detector and following the CIPAC 667/TC/M method.

The validation of this method was considered in compliance with SANCO/3030/99 rev.4.

Validation data:

|  |  |
| --- | --- |
| Specificity | To demonstrate the specificity of the method, several solutions are analyzed:   * Solvent blank (acetonitrile) * Formulation blank * Reference item of the active substance IR3535 * Test item of the product   No interference was found: no peak appears in the solvent blank and in the formulation blank, one peak is observed at the same retention time for the reference item and test item. |
| Linearity | Linearity is acceptable. |
| Precision | Repeatability is acceptable. |
| Accuracy | Accuracy was determined by analysis of 2 reconstituted samples. The accuracy results are expressed as the recovery rate. Accuracy is acceptable.   |  |  |  |  |  | | --- | --- | --- | --- | --- | | Fortification level | Recovery rate | Mean recovery rate | RSD (%) | n | | 9760 mg/L | 98.1%-98% | 98.1 % |  | 2 | | 6000 mg/L | 97.9-99.3% | 98.6 % |  | 2 | |

The analytical method is fully validated (the used method is a CIPAC) for the determination of the active substance IR3535 in the product.

META SPC 2: product reference 096587

Report: Anonymous 2015

Report no 15-912036-006

Test facility:

DEFITRACES

Z.A. des Andrés

150, rue Pré-Magne

69126 BRINDAS

FRANCE

Principle of the method:

Ethyl butylacetylaminopropionate (IR3535) is analysed after extraction from the formulation and quantified by gas chromatography with a FID detector and following the CIPAC 667/TC/M method.

The validation of this method was considered in compliance with SANCO/3030/99 rev.4.

Validation data:

|  |  |
| --- | --- |
| Specificity | To demonstrate the specificity of the method, several solutions are analyzed:   * Solvent blank (acetonitrile) * Formulation blank * Reference item of the active substance IR3535 * Test item of the product   No interference was found: no peak appears in the solvent blank and in the formulation blank, one peak is observed at the same retention time for the reference item and test item. |
| Linearity | Linearity is acceptable. |
| Precision | Repeatability is acceptable. |
| Accuracy | Accuracy was determined by analysis of 2 reconstituted samples. The accuracy results are expressed as the recovery rate. Accuracy is acceptable.   |  |  |  |  |  | | --- | --- | --- | --- | --- | | Fortification level | Recovery rate | Mean recovery rate | RSD (%) | n | | 9800 mg/L | 101.3%-101.7% | 101.5 % |  | 2 | | 5830 mg/L | 100.2% | 100.2 % |  | 2 | |

The analytical method is fully validated (the used method is a CIPAC) for the determination of the active substance IR3535 in the product.

Analytical methods for IR3535 residues in soil, air, water (drinking water) and sediment are available in Assessment Report of IR3535 Product-type 19, 13.03.2014. The applicant JUVA SANTE has a Letter of Access from Merck for these data.

**Analytical methods for the active substance**

|  |  |
| --- | --- |
| Technical active substance (principle of method) | Gas-chromatography with flame ionisation detection |
| Impurities in technical active substance (principle of method) | Gas-chromatography with flame ionisation detection |

**Analytical methods for residues**

|  |  |
| --- | --- |
| Soil (principle of method and LOQ) | Not required: significant residues of IR3535® in soil can be excluded. |
| Air (principle of method and LOQ) | Not required: IR3535® -based insect repellents spray applications involve large droplets which are not respirable. |
| Water (principle of method and LOQ) | Solid phase extraction (SPE) and UPLC-MS/MS detection (LOQ = 0.1 µg/L) |
| Body fluids and tissues (principle of method and LOQ) | Not required: IR3535® is not classified as toxic. |
| Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) | Not required: IR3535®-based insect repellent products are not used in a manner which may cause contact with such materials. |
| Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) ( | Not required: IR3535®-based insect repellent products are not used in a manner which may cause contact with such materials. |

Method for determination of IR3535 in water:

**Buttler O. (2012),** Study n° CRA14171, Doc n°435-001.

Principle:

Solid phase extraction (SPE) on Chromabond C18ec cartridges (conditioned with 5 mL methanol, after that 5 mL HPLC water + 0.1 % formic acid). The cartridges were washed with 2 mL HPLC water. After drying, the cartridges were eluted with 5 mL methanol. The eluates were sampled in a measuring flask (10 mL) and filled up to the mark. 0.5 mL of the eluate were diluted with 0.5 mL HPLC water in a vial. This procedure results in an enrichment factor of 10. Then there is UPLC-MS/MS with ESI+:

IR3535 m/z=216-86

m/z=216-128

IR 3535 free-acid m/z=216-86

m/z=216-128

The method is validated for determination of IR3535 and IR 3535 free-acid in surface water with a LOQ = 0.1µg/L.

Based on the intended uses of the product, no contamination of the environment is foreseen. Analytical methods for IR3535 residues in soil, air and sediment are unnecessary.

As the active substance IR3535 is not classified Toxic or Very Toxic, an analytical method for the determination of IR3535 residue in human body fluids and tissues is unnecessary.

As the product JUVA REPULSIF is not intended to be used with surface in contact with food/feed of plant and animal origin, analytical method for the determination of IR3535 residue in food/feed of plant and animal origin is unnecessary.

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| **FR CA Conclusion on the methods for detection and identification of the product** |
| The analytical method is fully validated for the determination of the active substance IR3535 in the product. |

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| --- |
| **FR CA Conclusion on the methods for monitoring of residue of active substance in compartiments** |
| Analytical methods were provided at EU level for the determination of IR3535 residue in water with respectively LOQ = 0.1 µg/L.  IR3535 is not toxic (T) or very toxic (T+) active substance. Therefore, an analytical method in biological matrices is not required.  The product is not intended to be used on surface in contact with food/feed of plant and animal origin, analytical method for the determination of IR3535 in food/feed of plant and animal origin is not required. |

## Efficacy against target organisms

### Function and field of use

Main Group 03: Pest Control

Product Type 19: Repellents and attractants

The products of the BPF are presented as ready-for-use aerosol or sprays to be applied on human skin. The product is sprayed in the hand and then spread on the exposed area of the skin (*i.e.* face, neck, arms, hands and legs).

### Organisms to be controlled and products, organisms or objects to be protected

According to the uses claimed by the applicant, the products of the BPF REPULSIF JUVA INSECTES are intended to be used to repel arthropods. The target organisms to be controlled are:

* Aedes mosquitoes (*Aedes spp.*), development stage: adults;
* Anopheles mosquitoes (*Anopheles spp.*), development stage: adults;
* Culex mosquitoes (*Culex spp.*), development stage: adults;
* Sandflies (*Phlebotomus spp.*), development stage: adults;
* Ticks (*Ixodes ricinus*), development stage: nymphs and adults (Meta SPC 2 only).

The purpose of the biocidal products is to protect humans from bites.

The application rates recommended by the applicant are the following:

* Meta SPC 1 (aerosol): 5.83 g/ m².
* Meta SPC 2 (spray):
* 5.83 g/m² when used against mosquitoes and sandflies,
* 7.5 g/m² when used against ticks or when target organisms include ticks.

### Effects on target organisms, including unacceptable suffering

The active substance modifies the behaviour of the target organisms. It repels them from the normal feeding behaviour leading to feed blood. No unacceptable suffering of the target organisms is expected.

### Mode of action, including time delay

IR3535® has an active repellent effect as insects avoid entering regions with IR3535® vapours. The exact biochemical mode of action of IR3535® on insects is not well known yet, but it is most self-evident to assume that IR3535® has an olfactory-based effect.

No delay is observed between the treatment and the occurrence of the biocidal effect.

### Efficacy data

The applicant has submitted following efficacy studies for the Meta SPC 1 (aerosol application):

All efficacy studies have been performed with the degassed product

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Experimental data on the efficacy of the biocidal product against target organism(s)** | | | | | | | |
| **Function** | **Field of use envisaged** | **Test substance** | **Test organism(s)** | **Test method** | **Test system / concentrations applied / exposure time** | **Test results: effects** | **Reference** |
| Repellent | skin application | **Marie rose aerosol protection antimoustique**  Réf. 096560  Aerosol formulation without propellant gaz  => 14% IR3535 | *Aedes aegypti*  *Ae. albopictus*  *Culex pipiens*  *Anopheles gambiae*  200 adult females / cages of 64000 cm3 | WHO/HTM/NTD/WHOPES/2009.4 | Arm in cage  **1 g per 600 cm² => 16.67 g/m²**  3 minutes repeated every hour until the first landing and then every 30 minutes until proven inefficacy of the product.  10 volunteers  Normal conditions :  27°C 65%RH (Culex)  Tropical conditions 32°C 75% RH (*Anopheles* and *Aedes*) | Test item has proved a complete protection over a period of:  - 8H against *Ae. aegypti*, *Cx. pipiens*;  - 7,5H against *Ae. albopictus,* *An. gambiae*.  **Tested dose is not the claimed dose** | Serrano, 2015a  RI = 1 |
| Repellent | skin application | **Marie rose aerosol protection antimoustique**  Réf. 096560  Aerosol formulation without propellant gaz  => 13.8% IR3535 | *Ae. albopictus*  *An. gambiae*  *P. duboscqi*  200 adult females / cages of 64000 cm3 | WHO/HTM/NTD/WHOPES/2009.4 | Arm in cage  **0.35 g per 600 cm² => 5.83 g/m²**  5 minutes repeated every hour until the first landing and then every 30 minutes until proven inefficacy of the product.  10 volunteers  Tropical conditions 32°C 75% RH | Test item has proved a complete protection over a period of:  - 7.5H against *Ae. albopictus, P. duboscqi*;  - 7H against *An. gambiae*. | Serrano, 2015b  RI = 1 |

The applicant has provided the following statement:

Two doses have been tested with the aerosol formulation to assess mosquito repellency: 1g/600 cm2 (on *Ae. albopictus, Ae. aegypti, Cx. pipiens* and *An. gambiae*) and 0.35 g/600 cm2 (on *Ae. albopictus* and *A. gambiae*). The dose of 1g/600 cm2 was chosen in a first instance but led to non-managed risk that is why tests were performed again at a lower dose. The first test allowed nevertheless identifying the most aggressive targets (*Ae. albopictus* and *An. gambiae*), in order to reduce the number of trials in the second test. No significant difference in the efficacy duration has been observed between both doses on *Ae. albopictus* and *An. gambiae*. It was thus considered that the dose of 0.35 g/600 cm2 was also protective towards *Ae. aegypti* and *Cx. pipiens* bites. Overall 7 hours efficacy duration for the aerosol (which corresponded to the lowest protection durations) has been considered for all mosquito species and *Phlebotomus* *spp.* at the applied dose of 0.35 g/600 cm2.

FR CA accepts applicant’s arguments

For the Meta SPC 2 (spray application), the applicant has submitted following data:

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Experimental data on the efficacy of the biocidal product against target organism(s)** | | | | | | | |
| **Function** | **Field of use envisaged** | **Test substance** | **Test organism(s)** | **Test method** | **Test system / concentrations applied / exposure time** | **Test results: effects** | **Reference** |
| Repellent | skin application | **Marie Rose Spray anti-moustiques –** Réf. 096602  Spray formulation 20% IR3535 | *Ae. aegypti*  *Ae. albopictus*  *Cx. pipiens*  *An. gambiae*  *P. duboscqi*  200 adult females / cages of 64000 cm3 | WHO/HTM/NTD/WHOPES/2009.4 | Arm in cage  **Application rate: 0.35g per 600 cm² => 5.83 g/m²**  5 minutes repeated every hour until the first landing and then every 30 minutes until proven inefficacy of the product.  10 volunteers  Normal conditions :  27°C 65%RH (Culex)  Tropical conditions 32°C 75% RH (*Phlebotomus*, *Anopheles* and *Aedes*) | Test item has proved a complete protection over a period of:  - 6.5H against *Ae. aegypti,* *An. gambiae;*  - 7H against *Ae. albopictus, P. duboscqi;*  - 7.5H against *Cx. pipiens.* | *Serrano, 2016a*  RI = 1 |
| Repellent | skin application | **Marie Rose Spray anti-moustiques –** Réf. 096602  Spray formulation 20% IR3535 | *Ixodes ricinus*  5 adults and 5 nymphs per mouse  10 mice | Derivated from OPPTS 810.3700 (2010) | Ticks placed on an untreated zone 3 cm away from the treated mouse  **Application rate: 0,033 g / 44 cm² => 7.5 g/m²**  Records of the number of ticks crossing the separating line between the untreated area and the treated skin part.  Test conditions :  25°C 65%RH | Test item has proven a protection over a period of 6 hours against the adults (6.1h) and nymphs (6.3h) of the tick *Ixodes ricinus*. | *Serrano, 2016b*  RI = 2 |

Submitted tests permit to validate the efficacy of the productMarie Rose Spray anti-moustiques – Référence 096602 for use against mosquitoes (*Culex spp*., *Aedes spp*. and *Anopheles spp*.) and sandflies (*Phlebotomus spp*.) at the claimed application rate of 5.83 g/m² and the use against ticks (*Ixodes ricinus*) at the tested application rate of 7.5 g/m².

It has to be noted that for the Meta SPC 2, only the formulation of meta SPC 2a has been tested in these two tests. Claimed variations within meta-SPC consist in the addition of up to 1.5% of perfumes and soothing agents.

It cannot be excluded that soothing agents, which are also masking agents could also have an impact. According to the Commission Decision of 9 February 2006 amending Decision 96/335/EC establishing an inventory and a common nomenclature of ingredients employed in cosmetic products, a masking agent is defined as agent that “reduces or inhibits the basic odour or taste of the product”.

According to the applicant, in scope of the cosmetic regulation, masking properties of an ingredient is related to an odor included in the human-perceptible spectrum. The sensory system of humans and arthropods are very different. There is no evidence to support the fact that the cosmetically masking properties of menthol can also be applied to arthropods such as mosquitoes or ticks.

Concerning the potential active effect of menthol against arthropods as an attractant or repellent, menthol is neither supported nor used as a biocidal active substance.

Based on the arguments mentioned above, the applicant is of the opinion that the read across within meta-SPC 2 formulations is reasonably acceptable.

Based on argumentation proposed by the applicant, considering that co-formulants are not PT19 active substances and that variations are limited (less than 1.5 % of the composition), FR CA agrees and proposes to authorize all products within the meta-SPC 2.

The applicant states that sweating has no impact on the protection time. However, FR CA considers that data coming from the arm-in-cage test (Serrano 2016a) performed at 32 °C are not robust enough to conclude on this statement. Indeed, a qualitative assessment of sweating (evaluated with a scale of: 1 = no visible sweat, 2 = average visible sweat, 3 = important visible sweat) has been done on the 10 volunteers, one volunteer had no visible sweating whereas the other 9 had average to important sweating, these results don’t permit to conclude that sweating has no impact on the protection time.

|  |
| --- |
| **FR CA conclusion on the efficacy of the product** |
| FR CA conclude that data presented in the dossier demonstrate that:   * the product of the Meta SPC 1 (of the BPF FAMILLE JUVA RÉPULSIF INSECTES provides a protection time up to 7 hours against adult mosquitoes (*Culex spp*., *Aedes spp*. *Anopheles spp*.) and sandflies (*Phlebotomus spp*.). * the product “Marie Rose Spray anti-moustiques – Référence 096602” of the Meta SPC 2 of the BPF FAMILLE JUVA RÉPULSIF INSECTES provides a protection time up to 6.5 hours against adult mosquitoes (*Culex spp., Aedes spp. Anopheles spp*.) and sandflies (*Phlebotomus spp*.) and, up to 6 hours against adults and nymphs of the tick *Ixodes ricinus*. Variations of composition within meta SPC 2 are considered as limited. FR CA proposes to authorize all products within the meta-SPC 2 meta SPC 2.   It is to be noted that no claim has been made concerning efficacy on tropical tick species, so the use efficacy of this product against ticks in tropical areas is not demonstrated. |

### Occurrence of resistance and resistance management

Resistance to IR3535 is not reported up to date in the scientific literature.

To ensure a satisfactory level of efficacy and avoid the development of resistance in susceptible insect populations, the following general recommendations have to be implemented:

* Always read the label or leaflet before use and follow all the instructions provided.
* Respect the recommended application doses.
* The users should inform the registration holder if the treatment is ineffective.

Considering the importance of this active substance in vector control, the authorisation holder has to implement a monitoring of scientific literature toward the active substance IR3535. Results of this assessment must be submitted to the Competent Authorities (CA) or other appointed bodies involved in resistance management every 5 years.

### Known limitations

None

### Evaluation of the label claims

French competent authorities (FR CA) conclude that data presented in the dossier demonstrate that:

* the product of the Meta SPC 1 of the BPF FAMILLE JUVA RÉPULSIF INSECTES provides a protection time up to 7 hours against adult mosquitoes (*Culex spp., Aedes spp., Anopheles spp.*) and sandflies (*Phlebotomus spp.*).
* the products of the Meta SPC 2 of the BPF FAMILLE JUVA RÉPULSIF INSECTES provides a protection time up to 6.5 hours against adult mosquitoes (*Culex spp*., *Aedes spp*. *Anopheles spp*.), 7 hours against adult sandflies (*Phlebotomus spp.*) and, up to 6 hours against adults and nymphs of the tick *Ixodes ricinus*.

No claim has been made concerning efficacy on tropical tick species, so the efficacy of this product against ticks in tropical areas is not demonstrated.

The application rates validated are the following:

* Meta SPC 1 (aerosol formulation for skin application):

Mosquitoes (*Culex spp*., *Aedes spp*., *Anopheles spp*.), adult stage: 5.83 g/m²

Sandflies (*Phlebotomus spp*.), adult stage: 5.83 g/m²

* Meta SPC 2 (spray formulation for skin application):
* Mosquitoes (*Culex spp*., *Aedes spp*. *Anopheles spp*.), adult stage: 5.83 g/m²
* Sandflies (*Phlebotomus spp*.), adult stage: 5.83 g/m²
* Ticks (*Ixodes ricinus*), adult and nymph stages: 7.5 g/m²

***Conditions of use linked to efficacy assessment***

* Always read the label or leaflet before use and follow all the instructions provided.
* Respect the recommended application doses.
* Retreat after water exposure without exceeding the maximal recommended application number.
* The user should inform the registration holder if the treatment is ineffective.
* The use of the product with other repellent products is not recommended.
* In case of a concomitant use of the product with sunscreen), first apply the sunscreen and wait 20 minutes before the application of the product.
* The protection time is only indicative. Environmental factors (e.g. high temperature, wind velocity) can modify it.

### Relevant information if the product is intended to be authorised for use with other biocidal product(s)

The biocidal products are not intended to be used with other biocidal products.

## Risk assessment for human health

### Assessment of effects on Human Health

***Skin corrosion and irritation***

No *in vitro* study is available for none of the biocidal products representative of the product family.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Summary table of animal studies on skin corrosion /irritation** | | | | | |
| **Method, Guideline,**  **GLP status, Reliability** | **Species, Strain, Sex, No/group** | **Test substance, Vehicle, Dose levels,  Duration of exposure** | **Results** | **Remarks** *(e.g. major deviations)* | **Reference** |
| OECD 404, GLP, Klimisch code 1 | 3 rabbits (males) NewZealand | Spray répulsif anti moustiques 8h Marie Rose - Ref 096602  Exposure during 4h, observation time 72h | Mean 24-72h, 3 rabbits:  Erythema: 0 Oedema: 0 | No deviation  No clinical effect reported. | Fagette (2007)  8.1 (a) Skin irritation or skin corrosion\_Spray |
| OECD 404, GLP, Klimisch code 1 | 3 rabbits (males) NewZealand | Spray 2 en 1 répulsif anti moustiques 8h Marie Rose - Ref 096587  Exposure during 4h, observation time 72h | Mean 24-72h, 3 rabbits:  Erythema: 0 Oedema: 0 | No deviation  No clinical effect reported. | Fagette (2008d)  8.1 (b) Skin irritation or skin corrosion\_Spray 2 en 1 |
| According to the French law Arrêté 9 juin 1992, not GLP, Klimisch code 4 | 6 rabbits(males) NewZealand | Spray Antimoustiques Réf. NIN006354  Similaire to the degasified aerosol  Exposure during 24h,  Observation time 1h and 48h after dressing removal | Mean 1-48h, 6 rabbits:  index of primary cutaneous irritation (total score at 1h + score at 48h)/24 : 0.1  Effects are observed in scarified skin, not in intact skin. | Not according to current guideline, exposure during 24h, observation lower than 72h | Dufour (1997)  Dufour (1997)  8.1 (c) Skin irritation or skin corrosion\_Aerosol |

*Rq: The tested products are representative products of meta SPC 2.*

Human data on skin corrosion/irritation: No human data is available for none of the Biocidal Products described in the present Assessment Report.

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Skin corrosion and irritation** | |
| Value/conclusion | Based on the available data, the products formulated within the ranges of the composition of the biocidal product family are considered as neither corrosive nor irritant to the skin. |
| Justification for the value/conclusion | This conclusion is supported by the available tests on products for meta SPC 2 and by the calculation using the conventional method as detailed in the CLP Annex I for meta SPC 1 and 2. |
| Classification of the product according to CLP | Not classified for skin corrosion/irritation according to CLP criteria. |

***Eye irritation***

No *in vitro* study is available for none of the biocidal products representative of the product family.

| **Summary table of animal studies on serious eye damage and eye irritation** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Method, Guideline,**  **GLP status, Reliability** | **Test substance, Doses** | **Relevant information about the study** | **Results** | **Remarks** *(e.g. major deviations)* | **Reference** |
| OECD 405 (2002),  GLP, Klimisch code 1 | 3 rabbits (males) NewZealand | Spray répulsif anti moustiques 8h Marie Rose - Ref 096602 | Mean 24-72h, 3 rabbits:  animal 1: Ch1.7 R2.7 I0 Co1.7  animal 2: Ch1 R2.3 I0 Co1.3  animal 3: Ch1.7 R3 I0.7 Co2  Reversibility: 8 days  The product is classified H319 | No deviation  No clinical effect reported. | Fagette (2008a)  8.2. (a) Eye irritation\_Spray |
| OECD 405 (2002),  GLP, Klimisch code 1 | 3 rabbits (males) NewZealand | Spray 2 en 1 répulsif anti moustiques 8h Marie Rose - Ref 096587 | Mean 24-72h, 3 rabbits:  animal 1: Ch1.3 R2.3 I0.3 Co1.7  animal 2: Ch1.3 R2.3 I0.3 Co1.7  animal 3: Ch1.3 R2.3 I0.3 Co1.7  Reversibility: 9 days  The product is classified H319 | No deviation  No clinical effect reported. | Fagette (2008c)  8.2. (b) Eye irritation\_Spray 2 en 1 |
| According to the French law Arrêté 9 juin 1992, not GLP, Klimisch code 4 | 3 rabbits(males) NewZealand | Spray Antimoustiques Réf. NIN006354  Similaire to the degasified aerosol  Observation time 7 days after instillation | Mean 24-72h, 3 rabbits:  animal 1:  Ch2.3R3 I1 Co1.7  animal 2: Ch1.7 R2.7 I1 Co1.7  animal 3: Ch0.33 R1.3 I0 Co0.7  Reversibility: not fully reversible at day 7 (end of the observation period) | Not according to current guideline, observation time limited à 7 days and all effects are not reversible | Dufour (1997)  8.2 (c) Skin irritation or skin corrosion\_Aerosol |

*Ch: chemosis R: redness I: iris C: cornea*

*Rq: The tested products are representative products of meta SPC 2.*

Human data on eye irritation: No human data is available for none of the Biocidal Products described in the present Assessment Report.

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Eye irritation** | |
| Value/conclusion | Based on the available data, the products formulated within the ranges of the composition of the biocidal product family are considered irritant to the eyes. |
| Justification for the value/conclusion | This conclusion is supported by the available tests on products for meta SPC 2 and by the calculation using the conventional method as detailed in the CLP Annex I for meta SPC 1and 2. |
| Classification of the product according to CLP | Classified for eye irritation according to CLP criteria, Eye Irrit. 2, H319. |

In this context, the product will not apply directly on the face. Spray the product in the hand and then spread it into the face.

***Respiratory tract irritation***

There is currently no testing requirement for respiratory irritation under the BPR (Reg (EU) No 528/2012). According to the CLP regulation (Reg (EC) No 1272/2008)) this parameter should be based primarily on human data.

Based on the available information and classification of components, the members of the Biocidal Product Family should not be considered as respiratory tract irritant.

|  |  |
| --- | --- |
| **Conclusion used in the Risk Assessment – Respiratory tract irritation** | |
| Justification for the conclusion | Based on an expert judgment :   * absence of human/animal data reported for this endpoint, * information on main components of the biocidal product family. |
| Classification of the product according to CLP | Based on the available information and classification of components, the members of the Biocidal Product Family should not be considered as respiratory tract irritant. |

***Skin sensitization***

No study (*in vitro*, *in vivo*) is available for none of the biocidal products representative of the product family. No human data are available either.

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Skin sensitisation** | |
| Value/conclusion | Not suspected to be a skin sensitiser |
| Justification for the value/conclusion | The sensitisation potency of the Biocidal Product Family is assessed according to the CLP regulation (Reg (EC) No 1272/2008 Annex I).  Based on the available data on the components, no classification is required. |
| Classification of the product according to CLP | Not classified. |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Skin sensitisation |
| Justification | The sensitisation potency of the Biocidal Product Family is assessed according to the CLP regulation (Reg (EC) No 1272/2008 Annex I).  Based on the available data on the components, no classification is required. |

***Respiratory sensitization (ADS)***

No data is available for respiratory sensitisation.

|  |  |
| --- | --- |
| **Conclusion** **used in Risk Assessment – Respiratory sensitisation** | |
| Value/conclusion | Not suspected to be a respiratory sensitiser |
| Justification for the value/conclusion |  |
| Classification of the product according to CLP and DSD | Not classified |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Respiratory sensitisation |
| Justification | According to Column 3 of the BPR regulation (Reg (EU) No 528/2012) Annex III, valid information is available on each component of the Biocidal Product Family allowing to apply the CLP criteria for classification (Section 3.4.3. CLP regulation (Reg (EC) No 1272/2008 Annex I). |

***Acute toxicity***

*Acute toxicity by oral route*

| **Summary table of animal studies on acute oral toxicity** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Method Guideline**  **GLP status, Reliability** | **Species, Strain, Sex, No/group** | **Test substance**  **Dose levelsType of administration** *(gavage, in diet, other)* | **Signs of toxicity** *(nature, onset, duration, severity, reversibility)* | **Value LD50** | **Remarks** *(e.g. major deviations)* | **Reference** |
| OECD 423, GLP, Klimisch code 1 | 6 rats (females) Sprague-Dawley) | Spray répulsif anti moustiques 8h Marie Rose - Ref 096602 | Slight clinical effects (piloerection) observed up to day 4 post dosing.  No mortality. | ≥ 2000 mg/kg bw | No deviation. | Fagette (2008b)  8.5.1 (a) Acute toxicity: oral\_Spray |
| OECD 423, GLP, Klimisch code 1 | 6 rats (females) Sprague-Dawley) | Spray 2 en 1 apaisant répulsif anti moustiques - Ref 096587 | No clinical effects recorded during the 14 days of observation.  No mortality. | ≥ 2000 mg/kg bw | No deviation. | Fagette (2008e)  8.5.1 (b) Acute toxicity: oral\_Spray |

*Rq: The tested products are representative products of meta SPC 2.*

No human data is available.

|  |  |
| --- | --- |
| **Value used in the Risk Assessment – Acute oral toxicity** | |
| Value | LD50 ≥ 2000 mg/kg bw |
| Justification for the selected value | Value obtained from 2 *in vivo* studies performed according to the test guideline OECD 423 on two products representatives of the Biocidal Product Family of meta SPC 2.  The calculation using the conventional method as detailed in the CLP Annex I leads to the same conclusion for meta SPC 1and 2 (not classified) |
| Classification of the product according to CLP | Not classified according to the CLP Regulation (Reg (EC) No 1272/2008). |

*Acute toxicity by inhalation*

No study (*in vitro*, *in vivo*) is available for none of the biocidal products representative of the product family. No human data are available either.

|  |  |
| --- | --- |
| **Value used in the Risk Assessment – Acute inhalation toxicity** | |
| Value | Not acutely toxic by inhalation. |
| Justification for the selected value | Based on the available information and classification of components, the members of the Biocidal Product Family should not be considered  acutely toxic by inhalation.. |
| Classification of the product according to CLP | Not classified |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Acute toxicity by inhalation. |
| Justification | The Acute toxicity by inhalation of the Biocidal Product Family is assessed according to the CLP regulation (Reg (EC) No 1272/2008 Annex I).  Based on the available data on the components, no classification is required. |

*Acute toxicity by dermal route*

No study (*in vitro*, *in vivo*) is available for none of the biocidal products representative of the product family. No human data are available either.

|  |  |
| --- | --- |
| **Value used in the Risk Assessment – Acute dermal toxicity** | |
| Value | Not acutely toxic by dermal route. |
| Justification for the selected value | Based on the available information and classification of components, the members of the Biocidal Product Family should not be considered  acutely toxic by dermal route. |
| Classification of the product according to CLP | Not classified |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Acute toxicity by dermal route. |
| Justification | The Acute toxicity by dermal route of the Biocidal Product Family is assessed according to the CLP regulation (Reg (EC) No 1272/2008 Annex I).  Based on the available data on the components, no classification is required. |

***Information on dermal absorption***

No study (in vitro, in vivo) is available on one member of the biocidal product family.

A read across with the dermal absorption value proposed in the CAR of IR3535 and supported by a study of Broschard *et al.*, 2013 (14%) was proposed by the applicant for the products family. The study of Broschard is summarised in the following table:

| **Summary table of on dermal absorption in human (in vivo)** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Method, Guideline,**  **GLP status, Reliability** | **Species, Number of skin samples tested per dose, Other relevant information about the study** | **Test substance, Doses** | **Absorption data for each compartment and final absorption value** | **Remarks** *(e.g. major deviations)* | **Reference** |
| No guideline followed, not under GLP, Klimisch code 2 | Human (5 males, 5 females), exposed to 3g of a formulation (20% IR3535)  Blood and urine samples were taken up to 24h after application (blood) and 48h (urine)  Analyses of IR3535 and its only metabolite (IR3535-free acid) were done by HPLC | The test item is a formulation of IR3535 (20%) characteristic of commercial products. | Based on the urine level (major route of excretion), the dermal absorption is 13.3%. | See below  . | Broschard *et al.*, 2013  8.6 (a) |

However, this study may underestimate dermal absorption because:

* a recovery rate is not proposed,
* the samples are taken only from urine and blood (for example faeces samples are not realised),
* the distribution of the active substance in the skin and the amount remaining in the skin is not determined.

For products of meta SPC 2, the formulations are close to the one described in the CAR. In this context, the read across is acceptable and the value of 14 % will be used for risk assessment.

However, for meta SPC 1 after evaporation of propellant, the product is composed essentially of active substance (15%) (at dilution inferior to active substance content of product in the CAR (20%)) and ethanol. As the product proposed in the CAR is composed of ethanol, emulsifier, solubilizer but also water, the read-across is not acceptable. Therefore, the default value of 25% will be used for risk assessment.

|  |  |
| --- | --- |
| **Value(s) used in the Risk Assessment – Dermal absorption** | |
| Substance | IR3535 |
| Value(s)\* | 25% (meta SPC 1) and 14% (meta SPC 2) |
| Justification for the selected value(s) | See before |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Dermal absorption. |
| Justification | A read across with value of CAR and Broschard study was proposed for family products. Broschard et al (2013) study is considered not acceptable.  The read across is accepted for meta SPC 2 but not for meta SPC 1. |

***Available toxicological data relating to non active substance(s) (i.e. substance(s) of concern)***

The assessment of the presence/absence of Substances of Concern (SoCs) related to health effect has been done according to the Annexe A of the ECHA Guidance Volume III Part B [[2]](#footnote-2).

The broad composition of the Biocidal Product Family includes no substance with health classification present above the threshold of classification according to the CLP Regulation (Reg (EC) 1272/2008), except the active substance itself and denatured alcohol (containing essentially ethanol and propan-2-ol).

Ethanol may be subject to a deeper assessment. Indeed, the Harmonised classification of ethanol (Index# 603-002-00-5) is Flam Liq 2 (H226). Depending on the supplier, the classification of the ethanol can be associated with an additional hazard class, Eye Irrit 2 (H319). This classification is agreed by several registrants of the Joint REACh Registration dossier[[3]](#footnote-3).

It has to be noted that this hazard class is similar to the one associated to the active substance (AS), IR3535®.

Due to the concentration of the AS in the Biocidal Product Family (>10%) in meta SPC 2, the Eye Irrit 2 (H319) is the appropriate classification to apply independently of any other co-formulants; which has been confirmed by the *in vivo* eye irritation tests (Fagette (2008a), Fagette (2008c), Dufour (1997)). In this context, no substance of concern is identified.

In meta SPC 1, the concentration in AS alone is not sufficient to induce a classification Eye Irrit 2 (H319). However, the presence of denatured alcohol at concentration superior to 10% induces this classification. Therefore, denatured alcohol (containing essentially ethanol and propan-2-ol) is considered as substance of concern.

In addition, due to hazard classification the Biocidal Product Family the risk management requirements regarding the classification Eye Irrit 2 (H319) is the application of the P statements as recommended in the Chapter 4 of the ECHA Guidance (Vol III-PartB, 2015). This approach corresponds to the “*banding evaluation scheme for classified SoCs*” as described in the Echa Guidance (Vol III-PartB, 2015) Annex A in case ethanol is classified as such.

Ethanol is also under evaluation as an Active Substance according to the BPR (Reg (EU) 528/2012). But no agreed draft final Competent Authorities Report (CAR) is available at the date of the submission of the present dossier.

Propan-2-ol is an active substance ever assessed according to the BPR (Reg (EU) 528/2012). Therefore, as it is present at concentration superior to 0.1% in the product, it is considered as SOC for meta SPC 1 and 2.

### Exposure assessment

**Identification of main paths of human exposure towards active substance(s) and substances of concern from its use in biocidal product**

| **Summary table: relevant paths of human exposure** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Exposure path** | **Primary (direct) exposure** | | | **Secondary (indirect) exposure** | | | |
| **Industrial use** | **Professional use** | **Non-professional use** | **Industrial use** | **Professional use** | **General public** | **Via food** |
| Inhalation | No | No | Yes | No | No | No | - |
| Dermal | No | No | Yes | No | No | Yes | - |
| Oral | No | No | No | No | No | Yes | Yes |

***List of scenarios***

The biocidal products are ready to use products (aerosol or spray) containing IR 3535 as active substance. In this context, no dilution or other preparation are necessary. They are applied directly to human skin of adults and children > 3 years to repel mosquitoes, phlebotomes and ticks. Application of the biocidal product must be done by adults only. It is considered that the exposure of the person spraying the product is covered by the exposure to the product he/she applies on his/her skin.

Two meta SPC are proposed by the applicant:

* Meta SPC 1: aerosol
* Meta SPC 2: spray.

For meta SPC 1 Aerosol, intended targets are mosquitoes and phlebotomes at the dose of 5.83 g/m2 of product. Two applications/ day are claimed for adults and children > 3 years.

For meta SPC 2 Spray, intended target are:

* Mosquitoes and phlebotomes at the dose of 5.83 g/m2 of product (2 applications/day for adults and 1 application/ day for children)
* Ticks at the dose of 7.5 g/m2 of product (1 application/day for adults and children)
* Mosquitoes, phlebotomes and ticks at the dose of 7.5 g/m2 of product (1 application/day for adults and children).

According to consumer spraying model 2 for trigger spray, the user will be exposed to 35.9 mg of product /m3 by inhlation during few minutes whereas he will be exposed to several g of product on skin with a dermal absorption of 14-25%. Therefore, inhalation exposure is considered negligible. and no additional data/assessment are required. The primary exposure is limited to the dermal route.

In order to determine the dermal exposure, the recommendation N°11 of BPC Ad hoc WG on human exposure[[4]](#footnote-4) is applied. Therefore, it is considered that the person will be exposed to the efficacy dose and wear a short sleeved shirt (T-shirt) and short.

The exposed body surface corresponds to 55% of the total body surface for an adult, as following N°11 of BPC Ad hoc WG on human exposure : head, neck, hands (palms and backs), arms (lower arms and 70% of upper arms), lower legs, 70% of thighs and 50% of feet.

The secondary exposure is limited to hand-to-mouth transfer. It is not expected to be a significant route of exposure.

Hand-to-mouth transfer behaviour is more frequent in small children and concerns mainly infants until 2-3 years. However, children from 3 years of age and adults may be accidentally exposed orally to the product. In this context, a reverse scenario calculation was included to estimate the percentage of the surface of the hands which can be put in the mouth to reach the AEL.

| **Summary table: scenarios** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Scenario** | **Primary or secondary exposure**  **Description of scenario** | **Exposed group** |
| Meta SPC 1 | | | |
| 1 | Application on the skin of Mosquitoes and phlebotome repellent | The biocidal products are applied directly to the skin at the dose of 5.83 g/m2:  The *primary exposure* is limited to the dermal route.  Body surface exposed: head, neck, hands (palms and backs), arms (lower arms and 70% of upper arms), lower legs, 70% of thighs and 50% of feet | General public.  Adult and child > 3 years. |
| Meta SPC 2 | | | |
| 2 | Application on the skin of Mosquitoes and phlebotome repellent | The biocidal products are applied directly to the skin at the dose of 5.83 g/m2:  The *primary exposure* is limited to the dermal route.  Body surface exposed: head, neck, hands (palms and backs), arms (lower arms and 70% of upper arms), lower legs, 70% of thighs and 50% of feet. | General public.  Adult and child > 3 years. |
| 3 | Application on the skin of ticks repellent or mosquitoes, phlebotome and tick repellent | The biocidal products are applied directly to the skin at the dose of 7.5 g/m2:  The *primary exposure* is limited to the dermal route.  Body surface exposed: head, neck, hands (palms and backs), arms (lower arms and 70% of upper arms), lower legs, 70% of thighs and 50% of feet | General public.  Adult and child > 3 years. |
| 4 | Exposure by hand to mouth transfer | Secondary exposure:  A reverse scenario was realised to estimate the percentage of the surface of the hands which can be put in the mouth to reach the AEL | General public.  Adult and child > 3 years. |

***Industrial exposure***

Not relevant

***Professional exposure***

Not relevant

***Non-professional exposure***

*Scenario [1-3]*

Scenario 1- 3 are scenario of application of the product on the skin. The difference between all these scenario are the application rate, active substance concentration in the product and dermal absorption value.

| **Description of Scenario [1-3]** | | |  |
| --- | --- | --- | --- |
| According to Recommendation 11 of ad hoc WG human exposure, it has been decided to assess exposure to the insect repellent based on the application rate.  The surface area to be considered is described as follow: ”It is considered that the exposed body surface area of an adult represents 55% of the total body surface (derived using the values of the body part surface areas from the HEAdhoc Recommendation 14). This corresponds to the situation when normal outdoor clothing (short-sleeved shirt (i.e. T-shirt) and shorts) are worn. This type of clothing leaves the following body parts exposed: head, neck, hands (palms and backs), lower arms, lower legs, feet and 70% of upper arms and thighs.”  Based on this repartition, for each age group the surface area was calculated. (see parameters below).  The exposure by dermal route after one application can be calculated according to the following equation:  where:  ID Internal dose (mg/kg b.w./day)  ARp Average dose of product applied on skin (mg/cm²)  CIR3535 Average concentration of substance in product (%)  BS Body surface exposed to the product (cm²)  DA Dermal absorption (%)  BW Body weight (kg)  This equation can be applied to adults and children. | | | |
|  | Parameters | Value | Reference |
| **Common parameters between all scenario (1-3)** | | |  |
|  | Body surface exposed to the product for **adult** considering exposure to head, neck, hands (palms and backs), arms (lower arms and 70% of upper arms), lower legs, 70% of thighs and 50% of feet. (cm2) | 9023 | Recommendation 14 of ad hoc WG human exposure |
| Body surface exposed to the product for **child (6-11 years)** considering exposure to head, neck, hands (palms and backs), arms (lower arms and 70% of upper arms), lower legs, 70% of thighs and 50% of feet. (cm2) | 4794 | Recommendation 14 of ad hoc WG human exposure |
| Body surface exposed to the product for **child (3-6 years)** head, neck, hands (palms and backs), arms (lower arms and 70% of upper arms), lower legs, 70% of thighs and 50% of feet. (cm2) | 3565 | Recommendation 14 of ad hoc WG human exposure |
| Tier 1 and 2 | Body weight of an **adult** (kg) | 60 | Recommendation 14 of ad hoc WG human exposure |
| Body weight of **child (6-11 years)** (kg) | 23.9 | Recommendation 14 of ad hoc WG human exposure |
| Body weight of **child (3-5 years)** (kg) | 15.6 | Recommendation 14 of ad hoc WG human exposure |
| **Specific parameters** | | | |
| Scenario 1 (meta SPC1) | Average dose of product applied on skin (g/m2) | 5.83 | Applicant data |
| Average concentration of substance in product (%) | 14.94 | Applicant data (concentration after vaporation of gas propellent) |
| Dermal absorption (%) | 25 | Default value |
| Scenario 2  (meta SPC2) | Average dose of product applied on skin (g/m2) | 5.83 | Applicant data |
| Average concentration of substance in product (%) | 20 | Applicant data |
| Dermal absorption (%) | 14 | Applicant data |
| Scenario 3  (meta SPC2) | Average dose of product applied on skin (g/m2) | 7.5 | Applicant data |
| Average concentration of substance in product (%) | 20 | Applicant data |
| Dermal absorption (%) | 14 | Applicant data |

**Calculations for Scenario [1-3]**

| **Summary table: systemic exposure from non-professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake** | **Estimated dermal uptake**  **mg/kg/d** | **Estimated oral uptake** | **Estimated total uptake**  **mg/kg/d** |
| Scenario [1]  adult | Tier 1 | NR | 3.27 | NR | 3.27 |
| Scenario [1]  child 6-11 years | Tier 1 | NR | 4.37 | NR | 4.37 |
| Scenario [1]  child 3-5 years | Tier 1 | NR | 4.98 | NR | 4.98 |
| Scenario [2]  adult | Tier 1 | NR | 2.45 | NR | 2.45 |
| Scenario [2]  child 6-11 years | Tier 1 | NR | 3.27 | NR | 3.27 |
| Scenario [2]  child 3-6 years | Tier 1 | NR | 3.73 | NR | 3.73 |
| Scenario [3]  adult | Tier 1 | NR | 3.16 | NR | 3.16 |
| Scenario [3]  child 6-11 years | Tier 1 | NR | 4.21 | NR | 4.21 |
| Scenario [3]  child 3-5 years | Tier 1 | NR | 4.80 | NR | 4.80 |

*Combined scenarios*

Not relevant

***Exposure of the general public***

*Scenario [4]*

| **Description of Scenario [4]** | | | | |
| --- | --- | --- | --- | --- |
| A reverse scenario is performed to determine the percentage of the surface of the hands which can be put in mouth to reach the AEL | | | | |
|  | | Parameters1 | Value |  |
| **Common to all population** | | | |  |
| Tier 1 | AEL (mg/kg/d) | | 5 | CAR |
| Oral absorption (%) | | 100 | CAR |
| **Common parameters for all uses** | | | |  |
| Tier 1 | Body weight of an **adult** (kg) | | 60 | Recommendation 14 of ad hoc WG human exposure |
| Body weight of **child (6-11 years)** (kg) | | 23.9 | Recommendation 14 of ad hoc WG human exposure |
| Body weight of **child (3-6 years)** (kg) | | 15.6 | Recommendation 14 of ad hoc WG human exposure |
| Surface of one hand of an **adult** (cm2) | | 410 | Recommendation 14 of ad hoc WG human exposure |
| Surface of one hand of a **child (6-11 years)** (cm2) | | 214 | Recommendation 14 of ad hoc WG human exposure |
| Surface of one hand of a **child (3-6 years)** (cm2) | | 165.45 | Recommendation 14 of ad hoc WG human exposure |
| **Specific parameters** | | | | |
| Meta SPC 1 | Average dose of product applied on skin (g/m2) | | 5.83 | Applicant data |
| Average concentration of substance in product (%) | | 14.94 | Applicant data |
| Meta SPC 2 (worst case) | Average dose of product applied on skin (g/m2) | | 7.5 | Applicant data |
| Average concentration of substance in product (%) | | 20 | Applicant data |

**Calculations for Scenario [4]**

| **Summary table: systemic exposure from non-professional uses** | | | | |
| --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Amount of product which can be ingested to reach AEL**  **mg** | **Skin surface which can be put in mouth**  **(cm2)** | **Percentage of the surface of the hand which can be put in mouth** |
| Meta SPC 1 | | | | |
| Scenario [4] Adult | - | 2008 | 3444 | 840% |
| Scenario [4] child 6-11 years | - | 800 | 1372 | 641% |
| Scenario [4] child 3-5 years | - | 536 | 919 | 555% |
| Meta SPC 2 | | | | |
| Scenario [4] Adult | - | 1500 | 2000 | 488% |
| Scenario [4] child 6-11 years | - | 598 | 797 | 372% |
| Scenario [4] child 3-5 years | - | 400 | 533 | 322% |

***Summary of exposure assessment***

| **Scenarios and values to be used in risk assessment** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Exposed group**  **(e.g. professionals, non-professionals, bystanders)** | **Tier/PPE** | **Estimated total uptake** |
| **Meta SPC 1** | | | |
| Scenario [1a]  adult | Non professional | Tier 1 | 3.27 |
| Scenario [1a]  child 6-11 years | Non professional | Tier 1 | 4.37 |
| Scenario [1a]  child 3-6 years | Non professional | Tier 1 | 4.98 |
| **Meta SPC 2** | | | |
| Scenario [2a]  adult | Non professional | Tier 1 | 2.45 |
| Scenario [2a]  child 6-11 years | Non professional | Tier 1 | 3.27 |
| Scenario [2a]  child 3-5 years | Non professional | Tier 1 | 3.73 |
| Scenario [3a]  adult | Non professional | Tier 1 | 3.16 |
| Scenario [3a]  child 6-11 years | Non professional | Tier 1 | 4.21 |
| Scenario [3a]  child 3-5 years | Non professional | Tier 1 | 4.80 |

***Monitoring data***

No monitoring data is available for the biocidal products covered in the biocidal product family or surrogate products.

***Dietary exposure***

As regards to the intended use of the family product FAMILLE REPULSIF JUVA INSECTES on human skin a contamination of food cannot be excluded. As a consequence, a dietary risk assessment is proposed in framework of this dossier.

Residue definitions

IR3535 is the only active substance considers for the biocidal products of FAMILLE REPULSIF JUVA INSECTES. The parent compound, IR3535 (ethyl butylacetylaminopropionate**)** was the only compound considered relevant regarding the dietary exposure.

*List of scenarios*

| **Summary table of main representative dietary exposure scenarios** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Type of use1** | **Description of scenario** | **Subject of exposure2** |
| 1. | General public | Contamination of food with contact with palm of treated hands | All kind of food |

1 e.g. animal husbandry, food industry, professional use, residential use.

2 e.g. chicken, milk, beer

*Information of non-biocidal use of the active substance*

IR3535 is not known to be used in other areas.

*Estimating Livestock Exposure to Active Substances used in Biocidal Products*

Regarding the intended use of the products of FAMILLE REPULSIF JUVA INSECTES, no livestock exposure to IR3535 is expected.

*Estimating transfer of biocidal active substances into foods as a result of professional and/or industrial application(s)*

The product FAMILLE REPULSIF JUVA INSECTES is only intended as non-professional use.

*Estimating transfer of biocidal active substances into foods as a result of non-professional use*

**Scenario 1**

Scenario 1 was performed for toddler, child and adult considering reference values mentioned in HEEG opinion 17[[5]](#footnote-5).

The scenario is not considered relevant for infant (<1 year), as the diet of infant consists mainly of milk and puree food, the contamination from hand to food is very limited.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | toddler  1 - 2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | Adult |
| body weight (kg) | 10 | 12 | 16 | 23.9 | 60 |
| hands (palms and back of both hands) (cm2) | 230.4 | 297 | 415 | 427.8 | 820 |

These biocidal products are intended for child > 3 years and adult, with a use **until 2 applications per day**. So, the exposure of child, adult and nevertheless also for toddlers is estimated in framework of this dossier.

To estimate dietary exposure, the following assumption and reference values were used:

|  |  |
| --- | --- |
| Ratio surface factor of the palm compared to whole hand | 0.5 |
| transfer factor (hand to food) in % | 100% |
| transfer factor (food to mouth) in % | 100% |
| handwash after use (i.e rinsing factor)[[6]](#footnote-6) | 1 (considering that no recommendation to wash hands is proposed) |

Considering the intended use of FAMILLE REPULSIF JUVA INSECTES, its concentration of IR3535, and the reference values mentioned above, the exposure was estimated as:

* Meta-SPC 1 - Use # 1 – **Mosquitoes**+Phlebotomes / Aerosol / Skin

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Product application rate (mg product/cm²) (effective) | 0.583 | | | | |
| Concentration (a.s in % w/w in the product) | 15 | | | | |
| Applied active substance (mg a.s/cm²) (effective) | 0.087 | | | | |
| age | Toddler  1-2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | adult |
| hands (palms and back of both hands) (cm2) | 230 | 297 | 415 | 428 | 820 |
| Intended number of application  (evaluated) | 0 (1 and 2) | 0 (1 and 2) | 2 | 2 | 2 |
| Ratio surface factor of the palm compared to whole hand | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| Food exposure per application (a.s in mg) | 10 | 13 | 18 | 19 | 36 |
| transfer factor (hand to food) in % | 100 | 100 | 100 | 100 | 100 |
| transfer factor (food to mouth) in % | 100 | 100 | 100 | 100 | 100 |
| ingested a.s in mg and per application | 0 | 0 | (18) | (19) | (36) |
| **total ingested a.s in mg** | (10 or 20) | (13 or 26) | **36** | **37** | **72** |
| Body weight in kg | 10 | 12 | 16 | 23.9 | 60 |
| Exposure per application in mg a.s/kg b.w./day | 0 | 0 | (1.1) | (0.8) | (0.6) |
| **Total exposure in mg a.s/kg b.w./day** | (1.0 or 2.0) | (1.1 or 2.2) | **2.3** | **1.6** | **1.2** |

in bold : results related to intended uses

in parenthesis: estimations performed in framework of the assessment

Meta-SPC 2 - Use # 2– **Mosquitoes**+Phlebotomes / Spray / Skin

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Product application rate (mg product/cm²) (effective) | 0.583 | | | | |
| Concentration (a.s in % w/w in the product) | 20 | | | | |
| Applied active substance (mg a.s/cm²) (effective) | 0.117 | | | | |
| age | Toddler  1-2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | adult |
| hands (palms and back of both hands) (cm2) | 230 | 297 | 415 | 428 | 820 |
| Intended number of application  (evaluated) | 0 (1 and 2) | 0 (1 and 2) | 1 (2) | 1 (2) | 2 |
| Ratio surface factor of the palm compared to whole hand | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| Food exposure per application (a.s in mg) | 13 | 17 | 24 | 25 | 48 |
| transfer factor (hand to food) in % | 100 | 100 | 100 | 100 | 100 |
| transfer factor (food to mouth) in % | 100 | 100 | 100 | 100 | 100 |
| ingested a.s in mg and per application | **0** | **0** | **24** | **25** | 48 |
| **total ingested a.s in mg** | (13 or 27) | (17 or 35) | (48) | (50) | **96** |
| Body weight in kg | 10 | 12 | 16 | 23.9 | 60 |
| Exposure per application in mg a.s/kg b.w./day | 0 | 0 | **1.5** | **1.0** | 0.8 |
| **Total exposure in mg a.s/kg b.w./day** | (1.3 or 2.7) | (1.4 or 2.9) | (3.0) | (2.1) | **1.6** |

in bold : results related to intended uses

in parenthesis: estimations realised in framework of the assessment

* Meta-SPC 2 - Use # 3 –and Use # 4 – **Mosquitoes**+Phlebotomes**+Ticks** / Spray / Skin

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Product application rate (mg product/cm²) (effective) | 0.75 | | | | |
| Concentration (a.s in % w/w in the product) | 20 | | | | |
| Applied active substance (mg a.s/cm²) (effective) | 0.150 | | | | |
| age | Toddler  1-2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | adult |
| hands (palms and back of both hands) (cm2) | 230 | 297 | 415 | 428 | 820 |
| Intended number of application  (evaluated) | 0 (1 and 2) | 0 (1 and 2) | 1 (2) | 1 (2) | 1 (2) |
| Ratio surface factor of the palm compared to whole hand | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| Food exposure per application (a.s in mg) | 17 | 22 | 31 | 32 | 62 |
| transfer factor (hand to food) in % | 100 | 100 | 100 | 100 | 100 |
| transfer factor (food to mouth) in % | 100 | 100 | 100 | 100 | 100 |
| **ingested a.s in mg and per application** | **0** | **0** | **31** | **32** | **62** |
| total ingested a.s in mg | (17 or 35) | (22 or 45) | (62) | (64) | (123) |
| Body weight in kg | 10 | 12 | 16 | 23.9 | 60 |
| Exposure per application in mg a.s/kg b.w./day | 0 | 0 | **1.9** | **1.3** | **1.0** |
| **Total exposure in mg a.s/kg b.w./day** | (1.7 or 3.5) | (1.9 or 3.7) | (3.9) | (2.7) | (2.1) |

in bold : results related to intended uses

in parenthesis: estimations realised in framework of the assessment

**Conclusion**

As regards the intended use of the products of FAMILLE REPULSIF JUVA INSECTES on human skin, and based on the assumptions and the reference values used, an estimation of dietary exposure for toddler, child and adult was performed. These estimations are considered as a worst case using the assumption that all the active substance from the palm hands will be ingested. The exposures via food range from 1.0 to 2.3 mg/kg bw/d for child (3-11 years old) and from 1.0 to 1.6 mg/kg bw/d for adult.

***Exposure associated with production, formulation and disposal of the biocidal product***

*Not relevant*

***Aggregated exposure***

*Not relevant*

### Risk characterisation for human health

**Reference values to be used in Risk Characterisation**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Reference** | **Study** | **NOAEL (LOAEL)** | **AF** | **Correction for oral absorption** | **Value** |
| AELshort-term | Rabbit, oral, 28- days toxicity study. | 500 mg/kg/d | 100 | 100 | 5 |
| AELmedium-term | Rabbit, oral, 28- days toxicity study. | 500 mg/kg/d | 100 | 100 | 5 |
| AELlong-term | Rabbit, oral, 28- days toxicity study. | 500 mg/kg/d | 100 | 100 | 5 |
| ARfD | Not applicable |  |  |  |  |
| ADI | Not applicable |  |  |  |  |

***Risk for industrial users***

Not relevant

***Risk for professional users***

Not relevant

***Risk for non-professional users***

**Systemic effects**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Task/**  **Scenario** | **Tier** | **AEL**  **mg/kg bw/d** | **Estimated uptake**  **mg/kg bw/d for 1 application per day** | **Estimated uptake/ AEL**  **(%)** | **Number of applications claimed by applicant** | **Number of applications acceptable\*** | **Acceptable**  **(yes/no) compared to applicant requirement** |
| **Meta SPC 1** | | | | | | | |
| Scenario [1]  adult | 1 | 5 | 3.27 | 65.5 | 2 | 1 | Only one application /day |
| Scenario [1]  child 6-11 years | 1 | 5 | 4.37 | 87.4 | 2 | 1 | Only one application /day |
| Scenario [1]  child 3-5 years | 1 | 5 | 4.98 | 99.5 | 2 | 1 | Only one application /day |
| Meta SPC 2 | | | | | | | |
| Scenario [2]  adult | 1 | 5 | 2.45 | 49.1 | 2 | 2 | Yes |
| Scenario [2]  child 6-11 years | 1 | 5 | 3.27 | 65.5 | 1 | 1 | Yes |
| Scenario [2]  child 3-5 years | 1 | 5 | 3.73 | 74.6 | 1 | 1 | Yes |
| Scenario [3]  adult | 1 | 5 | 3.16 | 63.2 | 1 | 1 | Yes |
| Scenario [3]  child 6-11 years | 1 | 5 | 4.21 | 84.2 | 1 | 1 | Yes |
| Scenario [3]  child 3-5 years | 1 | 5 | 4.80 | 96.0 | 1 | 1 | Yes |

\*The number of applications acceptable is determined by the ratio of (100% / % AEL for one application).

***Risk for the general public***

A reverse scenario is realised to determine the percentage of the surface of the hand which can be put in mouth to reach the AEL (cf exposure part).

For meta SPC 1 and meta SPC 2 more than 250 % of the hand can be put in the hand for adult and children. Therefore, the risk is considered acceptable.

Considering that head, neck, hands (palms and backs), arms (lower arms and 70% of upper arms), lower legs, 70% of thighs and 50% of feet are exposed, the conclusions on human health are the following::

For meta SPC 1

* For the application of the product against mosquitoes and phlebotomes, the risk is acceptable for adult and children from 3 years old for one application only. The claimed two applications lead to unacceptable risk.

For meta SPC 2:

* + For the application of the product against mosquitoes and phlebotomes, the risk is acceptable for adult and children from 12 years old for two applications as claimed. The risk for children between 3 and 11 years is acceptable for one application as claimed.
  + For the application of the product against ticks, , the risk is acceptable for adult and children between 3 and 11 years for one application (as required by applicant).

|  |  |  |
| --- | --- | --- |
| **Applications instructions** | | |
| Meta SPC 1 against  mosquitoes and sandlies | Meta SPC 2 against  mosquitoes  and sandlies | Meta SPC 2 against ticks |
| For adult: 1 second/head, 0.2 second/neck, 0.9 second/arm (lower and 70% of upper), 0.4 second/hand, 2.1 second/legs (lower and 70% of thigh) and 0.3 second/feet (50% of feet)  For children (6 -11 years old)-: 0.5 second/head, 0.2 second/neck, 0.5 second/arm (lower and 70% of upper), 0.2 second/hand, 1.1 second/legs (lower and 70% of thigh) and 0.1 second/feet (50% of feet)  For children (3-5 years old) : 0.5 second/head, 0.2 second/neck, 0.4 second/arm (lower and 70% of upper), 0.2 second/hand, 0.7 second/legs (lower and 70% of thigh) and 0.1 second/feet (50% of feet) | For dult: 3.9 stroke/head, 0.8 stroke/neck, 3.4 stroke/arm (lower and 70% of upper), 1.4 stroke/hand, 7.7 stroke/legs (lower and 70% of thigh) and 1 stroke/feet (50% of feet)  For children (6 -11 years old)-: 1.9 stroke/head, 0.9 stroke/neck, 1.8 stroke/arm (lower and 70% of upper), 0.8 stroke/hand, 3.9 stroke/legs (lower and 70% of thigh) and 0.5 stroke/feet (50% of feet)  For children (3-5 years old) : 1.8 stroke/head, 0.8 stroke/neck, 1.4 stroke/arm (lower and 70% of upper), 0.6 stroke/hand, 2.6 stroke/legs (lower and 70% of thigh) and 0.4 stroke/feet (50% of feet) | For adult: 5 stroke/head, 1 stroke/neck, 4.4 stroke/arm (lower and 70% of upper), 1.9 stroke/hand, 9.9 stroke/legs (lower and 70% of thigh) and 1.3 stroke/feet (50% of feet)  For children (6 -11 years old)-: 2.4 stroke/head, 1.1 stroke/neck, 2.3 stroke/arm (lower and 70% of upper), 1.0 stroke/hand, 5.1 stroke/legs (lower and 70% of thigh) and 0.7 stroke/feet (50% of feet)  For children (3-5 years old) : 2.4 stroke/head, 1.1 stroke/neck, 1.7 stroke/arm (lower and 70% of upper), 0.7 stroke/hand, 3.4 stroke/legs (lower and 70% of thigh) and 0.5 stroke/feet (50% of feet) |

**Authorisation based on article 19 (5) in France:**

Given the risk of vector-borne diseases transmission in France, FR CA considers that the biocidal familly product FAMILLE JUVA REPULSIFS INSECTES could be authorized for application on humans, with appropriate risk mitigation measures that limit human exposure based on article 19(5). The following RMMs are considered as applicable in France:

* For adult: “apply on the *face, neck, hands, ¾ arms, ½ legs once a day”*
* For children: “*do not apply the product on hands of children” and “*“apply on the *face, neck, ¾ arms, ½ legs and feet once a day”*

The estimation of exposure is performed considering that wearing a T shirt and short leads to an exposure of head, hand, ¾ arm and ½ legs (38 % of body surface for an adult)

The scenario and parameters are similar to the scenario assessed above except exposed area. Indeed, the *primary exposure* is limited to the body surface: head, hand, ¾ arms and ½ legs.

| **Description of Scenario [1-3]** | | |  |
| --- | --- | --- | --- |
|  | Parameters | Value | Reference |
| **Common parameters between all scenario (1-3)** | | |  |
| National approach | Body surface exposed to the product for **adult** considering exposure to head, hand, ¾ arm and ½ legs (cm2) | 6298 | Heeg opinion 17 |
| Body surface exposed to the product for **child (6-11 years)** considering exposure to head, hand, ¾ arm and ½ legs (cm2) | 3280 | Heeg opinion 17 |
| Body surface exposed to the product for **child (3-5 years)** considering exposure to head, hand, ¾ arm and ½ legs (cm2) | 2985 | US EPA exposure factor Handbook |

**Calculations for Scenario [1-3]**

| **Summary table: systemic exposure from non-professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake** | **Estimated dermal uptake**  **mg/kg/d** | **Estimated oral uptake** | **Estimated total uptake**  **mg/kg/d** |
| Scenario [1]  adult | National approach | NR | 2.29 | NR | 2.29 |
| Scenario [1]  child 6-11 years | National approach | NR | 2.99 | NR | 2.99 |
| Scenario [1]  child 3-5 years | National approach | NR | 4.06 | NR | 4.06 |
| Scenario [2]  adult | National approach | NR | 1.71 | NR | 1.71 |
| Scenario [2]  child 6-11 years | National approach | NR | 2.24 | NR | 2.24 |
| Scenario [2]  child 3-5 years | National approach | NR | 3.05 | NR | 3.05 |
| Scenario [3]  adult | National approach | NR | 2.20 | NR | 2.20 |
| Scenario [3]  child 6-11 years | National approach | NR | 2.88 | NR | 2.88 |
| Scenario [3]  child 3-5 years | National approach | NR | 3.92 | NR | 3.92 |

***Risk for non-professional users***

**Systemic effects**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Task/**  **Scenario** | **Tier** | **AEL**  **mg/kg bw/d** | **Estimated uptake**  **mg/kg bw/d for 1 application per day** | **Estimated uptake/ AEL**  **(%)** | **Number of applications claimed by applicant** | **Number of applications acceptable\*** | **Acceptable**  **(yes/no) compared to applicant requirement** |
| **Meta SPC 1** | | | | | | | |
| Scenario [1]  adult | 2 | 5 | 2.29 | 45.7 | 2 | 2 | Yes  (2 applications/day) |
| Scenario [1]  child 6-11 years | 2 | 5 | 2.99 | 59.8 | 2 | 1 | Only one application /day |
| Scenario [1]  child 3-5 years | 2 | 5 | 4.06 | 81.3 | 2 | 1 | Only one application /day |
| Meta SPC 2 | | | | | | | |
| Scenario [2]  adult | 2 | 5 | 1.71 | 34.3 | 2 | 2 | Yes |
| Scenario [2]  child 6-11 years | 2 | 5 | 2.24 | 44.8 | 1 | 1 | Yes |
| Scenario [2]  child 3-5 years | 2 | 5 | 3.05 | 60.9 | 1 | 1 | Yes |
| Scenario [3]  adult | 2 | 5 | 2.20 | 44.1 | 1 | 1 | Yes |
| Scenario [3]  child 6-11 years | 2 | 5 | 2.88 | 57.6 | 1 | 1 | Yes |
| Scenario [3]  child 3-5 years | 2 | 5 | 3.92 | 78.4 | 1 | 1 | Yes |

\*The number of applications acceptable is determined by the ratio of(100% / % AEL for one application).

***Risk for consumers via residues in food***

**Maximum residue limits or equivalent**

Residue definitions

Residue definition is established as IR3535.

|  |  |  |  |
| --- | --- | --- | --- |
| **MRLs or other relevant reference values** | **Reference** | **Relevant commodities** | **Value** |
| ARfD | No value was proposed in CAR. However, in framework of this dossier the value of the AELacute (Rabbit, overall, developmental study/28-d study: NOAEL of 500 mg/kg/day divided by a standard assessment factor of 100) is used | food | 5 mg/kg/day |
| ADI | Not considered necessary regarding the intended uses |  |  |

As regards the intended use of the products of FAMILLE REPULSIF JUVA INSECTES on skin, and the ARfD (based on AEL) proposed for IR3535, the following dietary risk assessments were performed:

Meta-SPC 1 - Use # 1 – Mosquitoes+Phlebotomes / Aerosol / Skin

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| age | Toddler  1-2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | adult |
| Exposure per application in mg a.s/kg b.w./day | 0 | 0 | (1.1) | (0.8) | (0.6) |
| **Total exposure in mg a.s/kg b.w./day** | (1.0 or 2.0) | (1.1 or 2.2) | **2.3** | **1.6** | **1.2** |
| ARfD (mg a.s/kg b.w./day ) | 5 | 5 | 5 | 5 | 5 |
| % of ARfD (per application) | 0 | 0 | (23) | (16) | (12) |
| % of ARfD (in total) | (20 or 40) | (22 or 43) | **45** | **31** | **24** |

in bold : results related to intended uses

in parenthesis: estimations realised in framework of the assessment

* Meta-SPC 2 - Use # 2– Mosquitoes+Phlebotomes / Spray / Skin

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| age | Toddler  1-2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | adult |
| Exposure per application in mg a.s/kg b.w./day | 0 | 0 | **1.5** | **1.0** | 0.8 |
| **Total exposure in mg a.s/kg b.w./day** | (1.3 or 2.7) | (1.4 or 2.9) | (3.1) | (2.1) | **1.6** |
| ARfD (mg a.s/kg b.w./day ) | 5 | 5 | 5 | 5 | 5 |
| % of ARfD (per application) | 0 | 0 | **30** | **21** | (16) |
| % of ARfD (in total) | (27 or 54) | (29 or 58) | (60) | (42) | **32** |

in bold : results related to intended uses

in parenthesis: estimations realised in framework of the assessment

Meta-SPC 2 - Use # 3 –and Use # 4 – **Mosquitoes**+Phlebotomes**+Ticks** / Spray / Skin

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| age | Toddler  1-2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | adult |
| Exposure per application in mg a.s/kg b.w./day | 0 | 0 | **1.9** | **1.3** | **1.0** |
| **Total exposure in mg a.s/kg b.w./day** | (1.7 or 3.5) | (1.9 or 3.7) | (3.9) | (2.7) | (2.1) |
| ARfD (mg a.s/kg b.w./day ) | 5 | 5 | 5 | 5 | 5 |
| % of ARfD (per application) | 0 | 0 | **39** | **27** | **21** |
| % of ARfD (in total) | (35 or 69) | (37 or 74) | (78) | (54) | (41) |

in bold : results related to intended uses

in parenthesis: estimations realised in framework of the assement

**Conclusion**

As regards the intended uses of the products of FAMILLE REPULSIF JUVA INSECTES on human skin and based on the assumption and the reference values used, no dietary risk for adult and child is expected.

The applicant proposes the following label recommendations:

* Do not sum up the different use modalities
* Do not apply on child's hand.
* Do not use on child below 36 months.
* Do not use for pregnant or breast-feeding women.
* Do not spray on food-stuff or in a room where food-stuffs are stored.

Considering the BP the following label recommendations is considered sufficient regarding dietary risk assessment:

Avoid any direct or indirect contact with food and feed.

***Risk characterisation from combined exposure to several active substances or substances of concern within a biocidal product***

Not Relevant

|  |
| --- |
| **FR CA conclusion** |
| Considering the intended uses on human skin of FAMILLE JUVA REPULSIFS INSECTES, conclusions regarding risks for human health are the following:  Meta SPC 1 (product to be used against mosquitoes and sandflies)   * two applications per day (as claimed by the applicant) lead to unacceptable risk * the risk is acceptable for adult and children from 3 years for one application per day only.   Meta SPC 2 (product to be used against mosquitoes, sandflies and ticks):   * for the application of the product against mosquitoes and sandlies, the risk is acceptable for adult and children from 12 years for two applications per day. The risk for children between 3 and 11 years is acceptable for one application per day. * for the application of the product against ticks, the risk is acceptable for adult and children from 3 years for one application as claimed by the applicant.   ***IN FRANCE ONLY***  Given the risk of vector-borne diseases transmission in France, FR CA considers that the biocidal familly products FAMILLE JUVA REPULSIFS INSECTES can be authorized for application on humans, with appropriate risk mitigation measures that limit human exposure based on article 19(5). The following RMMs are considered as applicable in France:   * For adult: “apply on the face, neck, hands, ¾ arms, ½ legs and feet once a day” * For children: “do not apply the product on hands of children” and ““apply on the face, neck, ¾ arms, ½ legs and feet once a day”   Meta SPC 1:  With these additional RMMs, the risk for human health is acceptable for adult and children from 12 years old for two applications per day and for children between 3 and 11 years old for one application only. Due to the need to protect children from vector-borne diseases, the product will be authorized for two applications per day for children between 3 and 11 years old in risk areas, as it is authorized for adults.  Meta SPC 2:  With these additional RMMs,   * for the use against mosquitoes and sandflies the risk is acceptable for adult and children from 12 years old for two applications per day. The risk for children between 3 and 11 years is acceptable for one application. However, due to the vector-borne diseases and the presence of voectors all around the day and possiby at night, two applications per day for children between 3 and 11 years old will also be authorized in risk areas, as it is authorized for adults. * For the use against ticks, , the risk is acceptable for adult and children from 3 years for one application per day.   Considering the BP the following label recommendations is considered sufficient regarding dietary risk assessment: Avoid any direct or indirect contact with food and feed. |

## Risk assessment for animal health

Not concerned.

## Risk assessment for the environment

|  |
| --- |
| Please notice that the environmental risk assessment is reported as provided by the applicant. The FR CA position is presented in **green evaluation boxes at the end of each part of the environmental section.** |

From the composition of the different products constituting the family, none of the classified substances, other than the IR3535®, is in concentration sufficiently high to classify the products, neither individually, nor by additivity. Consequently, no substance of concern, other than the active substance, is present in the biocidal products covered by the family.

Furthermore, no synergistic interactions are likely to occur between the product components: none of the components of the product family are known or intended synergists, or enhance the uptake, the excretion/clearance of other components, or have structural similarities with known synergists...

**No new studies have been submitted on the biocidal products** since the products applied for authorisation are identical to the representative product in the CAR (products containing 20 % active substance) and the intended use is identical.

The environmental risk assessment will thus only focus on the active substance.

A new risk assessment has been performed, however, since, in the meantime, a new Emission Scenario Document dedicated to PT19 has been drafted.

|  |
| --- |
| **Infobox 1** – FR: No other substance than the active is considered as of concern in the products of the family REPULSIF JUVA INSECTES. |

### Effects assessment on the environment

Information relating to the ecotoxicity of the biocidal active substance (except from the CA report 13/03/2014):

No toxic effects where observed during the acute toxicity studies on fish (Brachydanio rerio), Daphnia magna and algae (Desmodesmus subspicatus) (LC50 >100 mg/L). Therefore IR3535® is considered as not toxic for the aquatic environment.

The effect on aerobic biological sewage treatment processes was assessed by determining inhibition of respiration of the micro-organisms present in activated sludge following 3 hours contact. No inhibitory effect on aquatic microbial activity was registered for IR3535® (EC50 > 1000 mg/L).

Long term aquatic tests were not required because no acute toxicity was observed for the aquatic environment and the substance is primarily emitted to the STP before reaching the aquatic environment. Besides the Sewage Treatment Plant (STP) simulation test showed an elimination of 99 % in the STP.

No marine species were tested based on the presence of studies performed on freshwater species, all suggesting low toxicity and because no major emissions to the marine environment are expected.

In the absence of any long-term toxicity endpoints and marine data, the TGD on Risk Assessment prescribes an assessment factor of 1000 for the freshwater environment and 10000 for the marine environment.

For the sediment compartment, there are also no toxicity data available. The PNECsediment was calculated based on equilibrium partitioning method and PNECwater.

No terrestrial toxicity tests were performed for IR3535®. Due to the method of application directly on the skin only limited and very local emissions to the soil are expected. IR3535® is not likely to become accumulated in the soil in large amounts. PNECsoil has been calculated based on the equilibrium partitioning method.

The physicochemical properties of IR3535® do not suggest that this substance will pose a risk to the atmospheric environment. Therefore no PNECs where calculated for this compartment.

The low BCF values suggest that IR3535® has a low bioaccumulation potential. Therefore the risk of secondary poisoning via ingestion of contaminated food (eg. earthworms or fish) by birds or mammals is also low and no avian dietary tests were required.

PNEC determination (not originally present in the AS CA Report):

|  |  |  |
| --- | --- | --- |
|  | Rationale | Value |
| PNEC aqua (mg/L) | 100 (the highest tested concentration inducing no toxicological effect) /1000 (default assessment factor when only short term data is available) | 0.1 |
| PNEC seawater (mg/L) | 100 (the highest tested concentration inducing no toxicological effect) /10 000 (default assessment factor when only short term data is available) | 0.01 |
| PNEC sediment (mg/kg wet weight) | By equilibrium partition method  PNEC sed = (Ksusp-water/RHOsusp)\*PNECwater\*1000  and KaOC=475.25 L/kg | 1.11 |
| PNEC seased (mg/kg wet weight) | By equilibrium partition method  PNEC sed = (Ksusp-water/RHOsusp)\*PNECseawater\*1000  and KaOC=475.25 L/kg | 0.11 |
| PNEC soil (mg/kg wet weight) | By equilibrium partition method  PNEC soil = (Ksoil-water/RHOsoil)\*PNECwater\*1000  and VP=0.15Pa and WS=70 000 mg/L | 0.85 |
| PNEC STP (mg/L) | 1000 (EC50 OCDE 209) / 100 | 10 |

|  |
| --- |
| **Infobox 2** – FR: We agree with the PNEC values presented by the applicant.  Regarding the PNEC STP, the CAR of IR3535 stated on a PNEC value equals to 100 mg/L applying an AF of 10 to the NOEC value (1000 mg/L). Nevertheless, as no effect was observed in the respiration inhibition test (OECD 209), both EC50 and NOEC are above the highest tested concentration of 1000 mg/L. In this specific case, FRCA agrees to use the lowest PNEC value (10 mg/L) as proposed by the applicant. It should also be noted, that there is no consequence on the risk characterisation ratios. |

***Foreseeable routes of entry into the environment on the basis of the use envisaged***

No substances of concern or any relevant components other than the active substance are present in the biocidal products. The intended use of biocidal products is identical to the one of the active substance. The foreseeable route of entry into the environment of the biocidal products and on which exposure scenarii were developed is the aquatic environment, through wastewater treatment plant via bathing and showering of treated people, and to surface water bodies via swimming of treated people.

### Exposure assessment

**General information**

|  |  |
| --- | --- |
| Assessed PT | PT 19: Insect repellent |
| Assessed scenarios | **Scenario 1**: Skin repellent, human skin application, release to wastewater via bathing and showering of treated people.  **Scenario 2**: Skin repellent, human skin application, release to surface water bodies via swimming of treated people. |
| ESD(s) used | Emission Scenario Document for Product Type 19 |
| Approach | The consumption based approach for insect repellents applied on human skin and garment is based on the post-consumer release prediction model according to PT 1 (van der Aa & Balk, 2004) with some modifications that have been included. |
| Distribution in the environment | Calculated based on TGD 2003 |
| Groundwater simulation | No simulation for leaching to groundwater was performed. |
| Confidential Annexes | NO |
| Life cycle steps assessed | Production: No  Formulation No  Use: Yes  Service life: No |
| Remarks |  |

|  |
| --- |
| **Infobox 3** – FR: We agree with the proposed scenarios. |

***Emission estimation***

Considering the information given in the CAR on the environmental emissions for the indoor application of IR3535® formulations through a dummy product containing 20 % active substance: “*The ESD for PT1 offers two scenarios, one based on estimated yearly tonnage and one based on average daily consumption. Emissions through both scenarios were calculated and the worst case emission – in this instance the average daily consumption scenario – was used during the rest of the risk assessment*.” and provided that the tonnage of the applicant for the active substance is higher than the tonnage of the applicant for the biocidal products, only the scenario based on average daily application was assessed, as provided in the new ESD dedicated to PT19, and considered as the worst case scenario.

**Scenario [1] Skin repellent, human skin application, release to wastewater via bathing and showering of treated people.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Input parameters for calculating the local emission** | | | |
| **Input** | **Value** | **Unit** | **Remarks** |
| Scenario 1:Skin repellent, human skin application, release to wastewater via bathing and showering of treated people | | | |
| Nappl: number of applications per day on human skin | 3 |  | As a worst case, since normally related to the effectiveness of the repellency action of an insect repellent, it should be 2 |
| AREAskin: surface area to be treated | 16 600 | cm2 | Default (given by HEEG, EC, 2013) |
| Fpenetr: market share of a repellent active substance | 0.5 |  | Default value |
| Finh: fraction of inhabitants using a skin repellent product | 0.2 |  | Default value |
| Nlocal: Number of inhabitants feeding one STP | 10 000 | eq | Default value |
| Qformappl: Consumption per application | 0.75 | mg.cm-2 | Corresponds to the applied quantity in the efficacy-ticks test |
| Fair: Fraction released to air | 0 |  | Default value |
| Fskin: Fraction dermally absorbed | 0 |  | Default value |
| Fwater: Fraction released to wastewater | 1 |  | Default value |

Calculations for Scenario 1: Skin repellent, human skin application, release to wastewater via bathing and showering of treated people

| **Resulting local emission to relevant environmental compartments and PECs** | | |
| --- | --- | --- |
| **Compartment** | **Results** | **Remarks** |
| Local emission Freshwater | 7.47 kg/d | Elocalwater = Nlocal • Nappl • Qformappl • AREAskin/garment • Cformweight • Finh •  Fwater • Fpenetr • 10-9 |
| PEC Freshwater | 0.00373 mg.l-1 | Local emission rate to wastewater (Elocalwater): 7.47 kg.d-1  Concentration of the substance in the STP influent: 3.73 mg.l-1  Concentration of the substance in the STP effluent Local : 0.0373  Concentration in surface water during episode: 0.00373 mg.l-1  PEClocalwater = Clocalwater (PEC regional, water is used as background concentration for the local scale when the exposure assessment is performed using the tonnage based approach). |
| PEC Freshwater sediment | 0.041 mg/kg ww | PEClocalsed = (Kpsusp-water / RHOsusp) \* PEClocalwater \* 1000  Kpsusp-water = Fwater-susp+Fsolid-susp\*(Kpsusp/1000)\*RHOsolid |
| PEC Seawater | 0.000373 mg.l-1 | PECseawater = PEClocal water/10 |
| PEC Seawater sediment | 0.0041 mg/kg ww | PECseawater sed= PEClocalsed/10 |
| PEC STP | 0.0373 mg.l-1 | PEC STP=Clocal effluent |
| PEC Soil | 0 | PEC local soil is calculated from the following exposure routes: application of sewage sludge in agriculture and dry and wet deposition from the atmosphere. Both routes are negligeable in the present situation (99% elimination in STP simulation test, 1% goes in water effluent). |

|  |
| --- |
| **Infobox 4 – FR:**  **For scenario 1 (indirect release after skin application)**, we agree with the evaluation proposed by the applicant, that is a worst case covering all the products of the family, considering an application rate of 0.75 mg product/cm2 for the product containing 200 g ai/kg.  It is worth noting the value for AREAskin has been revised recently (WGI2017) to a harmonized value of 10660 cm2. As the higher surface area (16600 cm2) proposed by the applicant does not change the conclusions, it was kept for the assessment. |

**Scenario [2] Skin repellent, human skin application, release to surface water bodies via swimming of treated people.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Input parameters for calculating the local emission** | | | |
| **Input** | **Value** | **Unit** | **Remarks** |
| Scenario 2: Skin repellent, human skin application, release to surface water bodies via swimming of treated people. | | | |
| Nswimmer: Daily number of swimmers | 1500 | [-] | Default value |
| Fswim: Fraction of swimmers using the repellent product | 0.1 | [-] | Default value |
| Nappl: Number of applications per day | 1 | [d-1] | Default value  The interlink between the number of applications and the efficacy of the product does not apply in this respect. |
| Fwaterbody: Fraction released to surface water body | 1 | [-] | Default value |
| Cformweight: Active substance in the product | 200 | g.kg-1 | Set value based on active substance concentration in the product of 20% (w/w) |
| Qformappl: Consumption per application | 0.75 | mg.cm-2 | Corresponds to the applied quantity in the efficacy-ticks test |
| AREAskin: Treated area of human skin | 16 600 | cm2 | Default value (given by HEEG, EC, 2013) |

Calculations for Scenario 2: Skin repellent, human skin application, release to surface water bodies via swimming of treated people.

| **Resulting local emission to relevant environmental compartments and PECs** | | |
| --- | --- | --- |
| **Compartment** | **Results** | **Remarks** |
| Local emission Freshwater | 0.374 kg/d | Elocalwater = Nswimmers • Nappl • Qformappl • AREAskin • Cformweight • Fswim • Fwaterbody • 10-9 |
| PEC Freshwater | 0.078 mg.l-1 | Local emission rate to wastewater (Elocalwater): 0.374 kg.d-1  Clocalwater,91d = Elocalwater \* Temission,91d / Vwaterbody = 7.8E-05 g.l-1; Temission,91d=91 d; Vwaterbody= 435000 m3,  As a first tier approach, the PEClocalwater corresponds to Clocalwater,91d from equation 3.14 of the ESD and should be used for the risk assessment, representing the worst-case situation. |
| PEC Freshwater sediment | 0.868 mg/kg ww | PEClocalsed = (Kpsusp-water / RHOsusp) \* PEClocalwater \* 1000  Kpsusp-water = Fwater-susp+Fsolid-susp\*(Kpsusp/1000)\*RHOsolid |
| PEC Seawater |  | Not relevant |
| PEC Seawater sediment |  | Not relevant |
| PEC STP |  | Not relevant |
| PEC Soil |  | Not relevant |

|  |
| --- |
| **Infobox 5 – FR:**  **For scenario 2 (direct release via swimming after skin application)**, we agree with the evaluation proposed by the applicant, that is a worst case covering all the products of the family, considering an application rate of 0.75 mg product/cm2 for the product containing 200 g ai/kg.  It is worth noting the value for AREAskin has been revised recently (WGI2017) to a harmonized value of 10660 cm2. As the higher surface area (16600 cm2) proposed by the applicant does not change the conclusions, it was kept for the assessment.  The exposure assessment has been conducted for highly infested areas, considering a fraction of swimmers using the repellent product of 0.1 that is also a worst case. |

***Fate and distribution in exposed environmental compartments***

| **Identification of relevant receiving compartments based on the exposure pathway** | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Fresh-water | Freshwater sediment | Sea-water | Seawater sediment | STP | Air | Soil | Ground-water | Other |
| Scenario 1 | Yes | Yes | Yes | Yes | Yes | NR | Yes | Yes |  |
| Scenario 2 | Yes | Yes | NR\* | NR\* | NR | NR | NR | NR |  |

*NR: not relevant*

*NR\*: To represent a realistic worst-case scenario, the release of repellents from the skin of treated humans into ponds, lakes or reservoirs during swimming was evaluated. Due to dilution effects, neither coastal areas nor rivers were considered in the context of the PT19 ESD.*

|  |  |  |  |
| --- | --- | --- | --- |
| **Input parameters for calculating the fate and distribution in the environment** (From active substance dossier) | | | |
| Input | Value | Unit | Remarks |
| Molecular weight | 215.29 |  |  |
| Vapour pressure (at 20°C) | 0.15 | Pa |  |
| Water solubility (at 20°C) | 70000 | mg/l |  |
| Log Octanol/water partition coefficient | 1.7 | Log 10 |  |
| Organic carbon/water partition coefficient (Koc) | 475.25 | l/kg |  |
| Henry’s Law Constant (at 25°C) | 6.08E-4 | Pa/m3/mol | Calculated |
| Biodegradability | Not ready biodegradable |  | From screening tests |
| Biodegradability | 99% elimination |  | From STP simulation test |
| DT50 for biodegradation in surface water |  | d or hr (at 12ºC) | Remains mainly in the water phase. There it was first rapidly degraded to its free acid, after which this metabolite ultimately degraded after a lag phase. |
| DT50 for hydrolysis in surface water |  | d or hr (at 12ºC /pH) | Hydrolysis only occurred slowly under alkaline conditions (DT50 = 176.5 h at 25 °C and pH 9 or 866.13 h at 12 °C). Under acidic and neutral conditions IR3535® is hydrolytically stable. |
| DT50 for photolysis in surface water |  | d or hr | No photolysis was observed in water |

|  |  |  |
| --- | --- | --- |
| **Calculated fate and distribution in the STP *[if STP is a relevant compartment]*** | | |
| Compartment | Percentage [%] | Remarks |
| Scenario 1 |  |
| Air |  |  |
| Water | 1 |  |
| Sludge |  |  |
| Degraded in STP | 99 | From STP simulation test |

|  |
| --- |
| **Infobox 6 – FR:**  We agree with the proposed values.  To complete the information, no degradation in water or sediment was considered for the swimming scenario and the cumulative concentration over 91 days was taken for the risk characterization as a worst case.  Concerning the distribution in the STP, the proposed values were accepted for the approval of the substance as a Tier 2 approach based on a STP simulation test, leading to no exposure of the terrestrial compartment (including groundwater). |

***Calculated PEC values***

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Summary table on calculated PEC values** | | | | | | |
|  | **PECSTP** | **PECwater** | **PECsed** | **PECseawater** | **PECseased** | **PECsoil** |
| [mg/l] | [mg/l] | [mg/kgwwt] | [mg/l] | [mg/kgwwt] | [mg/kgwwt] |
| Scenario 1 | 0.0373 | 0.0037 | 0.041 | 0.00037 | 0.0041 | 0 |
| Scenario 2 | NR | 0.078 | 0.868 | NR | NR | NR |

|  |
| --- |
| **Infobox 7 – FR:**  We agree with the PEC values for scenarios 1 (indirect release after skin application) and 2 (direct release via swimming after skin application). |

***Primary and secondary poisoning***

The IR3535® is unlike to bioaccumulate in aquatic or terrestrial environment according to the TGD. It has a low log Kow (1.7) and it is not highly adsorptive. For these reasons, primary and secondary poisoning assessments have been waived.

|  |
| --- |
| **Infobox 8 – FR:**  We agree with this waiving. |

### Risk characterisation

***Atmosphere***

Conclusion:IR3535® has a low potential for volatilisation. Consequently, exposure assessment and risk characterisation were not conducted for the atmosphere.

***Sewage treatment plant (STP)***

|  |  |
| --- | --- |
| **Summary table on calculated PEC/PNEC values** | |
|  | **PEC/PNECSTP** |
| Scenario 1 | 0.0373/10 = 0.0037 |
| Scenario 2 | Not relevant |

Conclusion: No risk is identified for the sewage treatment plant.

***Aquatic compartment***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Summary table on calculated PEC/PNEC values** | | | | |
|  | **PEC/PNECwater** | **PEC/PNECsed** | **PEC/PNECseawater** | **PEC/PNECseased** |
| Scenario 1 | 0.0037/0.1 = 0.037 | 0.041/1.11 = 0.037 | 0.00037/0.01 = 0.037 | 0.0041/0.11 = 0.037 |
| Scenario 2 | 0.078/0.1 = 0.78 | 0.868/1.11 = 0.78 | Not relevant | Not relevant |

Conclusion: No risk is identified fort the aquatic compartment.

***Terrestrial compartment***

|  |  |
| --- | --- |
| **Calculated PEC/PNEC values** | |
|  | **PEC/PNECsoil** |
| Scenario 1 | 0 |
| Scenario 2 | Not relevant |

Conclusion No risk is identified fort the aquatic compartment.

***Groundwater***

No simulation for leaching to groundwater was performed and consequently no risk characterisation was conducted for this compartment.

***Primary and secondary poisoning***

Primary and secondary poisoning

The IR3535® is unlike to bioaccumulate in aquatic or terrestrial environment according to the TGD. It has a low log Kow (1.7) and it is not highly adsorptive. For these reasons, primary and secondary poisoning assessment have been waived.

***Mixture toxicity***

Mixture toxicity is not relevant.

***Aggregated exposure (combined for relevant emmission sources)***

The two scenarii could be aggregated as a worst case.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Summary table on calculated ΣPEC/PNEC values** | | | | | |
| **ΣPEC/PNEC**  **STP** | **ΣPEC/PNEC**  **water** | **ΣPEC/PNEC**  **sed** | **ΣPEC/PNEC**  **seawater** | **ΣPEC/PNEC**  **seased** | **ΣPEC/PNECsoil** |
| 0.0067  (scen 1) | 0.85  (scen 1, 2) | 0.85  (scen 1, 2) | 0.0671  (scen 1) | 0.067  (scen 1) | 0  (scen 1) |

Conclusion: bases on aggregated exposure, there is no risk for any of the environmental compartments.

|  |
| --- |
| **Overall conclusion on the risk assessment for the environment of the product** |
| The use of the biocidal products does not induce risk for any of the environmental compartments. |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Infobox 9 – FR:**  We agree with the applicant conclusions. The aggregated risk assessment has been slightly revised.   |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | **Summary table on calculated ΣPEC/PNEC values** | | | | | | | **ΣPEC/PNEC**  **STP** | **ΣPEC/PNEC**  **water** | **ΣPEC/PNEC**  **sed** | **ΣPEC/PNEC**  **seawater** | **ΣPEC/PNEC**  **seased** | **ΣPEC/PNECsoil** | | 0.0037  (scen 1) | 0.82  (scen 1, 2) | 0.82  (scen 1, 2) | 0.067  (scen 1) | 0.067  (scen 1) | 0  (scen 1) |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | Type of application / Uses | Scenario | STP | Aquatic compartment (surface water and sediment) | Soil | Groundwater | Secondary Poisoning | | Human skin | Indirect release via bathing or showering  (Scenario 1) | Acceptable | Acceptable | Acceptable | Acceptable | n.r. | | Direct release via swimming  (Scenario 2) | n.r. | Acceptable | n.r. | n.r. | n.r. | | Aggregated exposure | n.r. | Acceptable | n.r. | n.r. | n.r. |   n.r. Not relevant |

## Measures to protect man, animals and the environment

Please see the summary of product characteristic (SPC).

## Assessment of a combination of biocidal products

Not concerned

## Comparative assessment

Not applicable in the present situation.

# Annexes

## List of studies for the biocidal product (family)

| Author(s) | IUCLID Section No. / Reference No. | Year | Title, Source (laboratory), Report No., GLP, (Un)Published | Data Protection (Yes/No) | Owner | Essential for the evaluation |
| --- | --- | --- | --- | --- | --- | --- |
| Anonymous | 3.1 Appearance | 2015a | Analytical certificate - MARIE ROSE SPRAY Réf 096602, GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 3.2 Acidity, alkalinity | 2015b | Physico-chemical tests and chemical analyses before and after an accelerated storage procedure for 8 weeks at 40 °C ± 2 °C on Marie Rose Spray 2 en 1 Réf 096587. Study report n°15-912036-004. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 3.2 Acidity, alkalinity | 2015c | Physico-chemical tests and chemical analyses before and after an accelerated storage procedure for 8 weeks at 40 °C ± 2 °C on Marie Rose Aérosol Réf 096560. Study report n°15-912036-009. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 3.3 Relative density | 2015d | Physico-chemical tests on Marie Rose aérosol Réf 096560. Study report n°15-912036-008. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 3.3 Relative density | 2015e | Physico-chemical tests on Marie Rose Spray 2 en 1 Réf 096587. Study report n°15-912036-003. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 3.3 Relative density | 2015f | Physico-chemical tests on Marie Rose Spray Réf 096602. Study report n°15-912036-001. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 3.4.1 Storage stability tests | 2015b | Physico-chemical tests and chemical analyses before and after an accelerated storage procedure for 8 weeks at 40 °C ± 2 °C on Marie Rose Spray 2 en 1 Réf 096587. Study report n°15-912036-004. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 3.4.1 Storage stability tests | 2015c | Physico-chemical tests and chemical analyses before and after an accelerated storage procedure for 8 weeks at 40 °C ± 2 °C on Marie Rose Aérosol Réf 096560. Study report n°15-912036-009. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Loufrani | Long term storage stability | 2020 | Physico-chemical tests and chemical stability after a storage procedure for 36 months at 20 °C ± 2 °C on 096587 - Spray répulsif apaisant moustique Marie Rose - serti and 096509 - Spray répulsif apaisant moustique Marie Rose - vissé | Yes | Laboratoires JUVASANTE | Yes |
| Anonymous | 3.5.12 Spraying pattern aerosol | 2015c | Physico-chemical tests and chemical analyses before and after an accelerated storage procedure for 8 weeks at 40 °C ± 2 °C on Marie Rose Aérosol Réf 096560. Study report n°15-912036-009. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Preterre D. | 3.5.13 Other technical characteristics: droplet size | 2015 | Analyse par diffraction de la lumière de la granulométrie de sprays. Study report n° de la commande G51-20150717. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Holtz, C. | 3.5.13 Other technical characteristics:internal pressure Marie Rose Aérosol | 2016 | Certificate of analysis: repellents Juva Santé | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 3.8 Surface tension | 2015e | Physico-chemical tests on Marie Rose Spray 2 en 1 Réf 096587. Study report n°15-912036-003. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 3.8 Surface tension | 2015d | Physico-chemical tests on Marie Rose aérosol Réf 096560. Study report n°15-912036-008. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 3.9 Viscosity | 2015f | Physico-chemical tests on Marie Rose Spray Réf 096602. Study report n°15-912036-001. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 3.9 Viscosity | 2015e | Physico-chemical tests on Marie Rose Spray 2 en 1 Réf 096587. Study report n°15-912036-003. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 3.9 Viscosity | 2015d | Physico-chemical tests on Marie Rose aérosol Réf 096560. Study report n°15-912036-008. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 4.1 Explosives | 2015e | Physico-chemical tests on Marie Rose Spray 2 en 1 Réf 096587. Study report n°15-912036-003. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 4.1 Explosives | 2015d | Physico-chemical tests on Marie Rose aérosol Réf 096560. Study report n°15-912036-008. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 4.6 Flammable liquids | 2015f | Physico-chemical tests on Marie Rose Spray Réf 096602. Study report n°15-912036-001. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 4.6 Flammable liquids | 2015e | Physico-chemical tests on Marie Rose Spray 2 en 1 Réf 096587. Study report n°15-912036-003. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 4.6 Flammable liquids | 2015d | Physico-chemical tests on Marie Rose aérosol Réf 096560. Study report n°15-912036-008. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Chambouvet, L. | 4.16 Corrosive to metals | 2015a | Determination of the corrosiveness of a solution in the presence of steel and aluminum alloy “Marie-Rose Spray 2 en 1 Réf 096587”. Study report n° PV/239/15/LC. Not GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Chambouvet, L. | 4.16 Corrosive to metals | 2015b | Determination of the corrosiveness of a solution in the presence of steel and aluminum alloy “Marie-Rose aerosol Réf 096560”. Study report n° PV/249/15/LC. Not GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 4.17.1 Auto-ignition temperature | 2015e | Physico-chemical tests on Marie Rose Spray 2 en 1 Réf 096587. Study report n°15-912036-003. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 4.17.1 Auto-ignition temperature | 2015d | Physico-chemical tests on Marie Rose aérosol Réf 096560. Study report n°15-912036-008. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 5. Methods of detection and identification | 2015g | Determination of the content of ethyl butylacetylaminopropionate in Marie Rose Spray Réf 096602. Study report n°15-912036-002. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 5. Methods of detection and identification | 2015h | Validation of the analytical method for the determination of ethyl butylacetylaminopropionate in Marie Rose Spray 2 en 1 Réf 096587 In compliance with SANCO/3030/99 rev. 4 from 11/07/00. Study report n°15-912036-006. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Anonymous | 5. Methods of detection and identification | 2015i | Validation of the analytical method for the determination of ethyl butylacetylaminopropionate in Marie Rose Aérosol Réf 096560 In compliance with SANCO/3030/99 rev. 4 from 11/07/00. Study report n°15-912036-011. GLP. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Serrano, B. | 6.7 Efficacy data to support these claims | 2015a | Laboratory assessment of a personal skin repellent against mosquitoes. Study report n° 1938/0515. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Serrano, B. | 6.7 Efficacy data to support these claims | 2016 | Laboratory assessment of a personal skin repellent against mosquitoes. **Erratum** to the Study report n° 1938/0515. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Serrano, B. | 6.7 Efficacy data to support these claims | 2015b | Laboratory assessment of a personal skin repellent against mosquitoes, Trial against *Aedes albopictus*, *Anopheles gambiae* and *Phlebotomus duboscqi*, Trial in tropical conditions. Study report n° 1994/0915R. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Serrano, B. | 6.7 Efficacy data to support these claims | 2016 | Laboratory assessment of a personal skin repellent against mosquitoes, Trial against *Aedes albopictus*, *Anopheles gambiae* and *Phlebotomus duboscqi*, Trial in tropical conditions. **Addendum** to the Study report n° 1994/0915R. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Serrano, B. | 6.7 Efficacy data to support these claims | 2016a | Laboratory assessment of a personal skin repellent against mosquitoes. Study report n° 2099/0616. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Serrano, B. | 6.7 Efficacy data to support these claims | 2016b | Laboratory assessment of a personal skin repellent against ticks. Study report n° 2099b/0616. | Yes | LABORATOIRES JUVA SANTE | Yes |
| Fagette | 8.1 Skin irritation/corrosion | 2007 | Effet irritant/corrosif aigu sur la peau chez le lapin - OCDE 404 - Element d'essai: Spray répulsif anti moustiques 8h Marie Rose - Ref 096602. Study report n° Tn 560/07-3543. GLP. | Yes | LABORATOIRES JUVA SANTE |  |
| Fagette | 8.1 Skin irritation/corrosion | 2008d | Effet irritant/corrosif aigu sur la peau chez le lapin - OCDE 404 - Element d'essai: Spray 2 en 1 apaisant repulsif Marie rose anti-moustiques - Ref 096587. Study report n° To 387/08-2817. GLP. | Yes | LABORATOIRES JUVA SANTE |  |
| Dufour | 8.1 Skin irritation/corrosion | 1997 | Etude de la tolérance locale du produit - Spray Antimoustiques Réf. NIN006354. Study report n° Td 493/97-1941. Not GLP. | Yes | LABORATOIRES JUVA SANTE |  |
| Fagette | 8.2 Eye irritation/corrosion | 2008a | Effet irritant/corrosif aigu sur l'œil chez le lapin - OCDE 405 - Element d'essai: Spray répulsif anti moustiques 8h Marie Rose - Ref 096602. Study report n° Tn 560/07-3543. GLP. | Yes | LABORATOIRES JUVA SANTE |  |
| Fagette | 8.2 Eye irritation/corrosion | 2008c | Effet irritant/corrosif aigu sur l'œil chez le lapin - OCDE 405 - Element d'essai: Spray 2 en 1 répulsif anti moustiques 8h Marie Rose - Ref 096587. Study report n° To 388/08-2817. GLP. | Yes | LABORATOIRES JUVA SANTE |  |
| Dufour | 8.2 Eye irritation/corrosion | 1997 | Etude de la tolérance locale du produit - Spray Antimoustiques Réf. NIN006354. Study report n° Td 493/97-1941. Not GLP. | Yes | LABORATOIRES JUVA SANTE |  |
| Fagette | 8.5.1 Acute toxicity: Oral | 2008b | Etude de la toxicité orale aigue chez le rat - Méthode par classe de toxicité Aiguë - OCDE 423 - Element d'essai: Spray répulsif anti moustiques 8h Marie Rose - Ref 096602. Study report n° Tn 561/07-3543. GLP. | Yes | LABORATOIRES JUVA SANTE |  |
| Fagette | 8.5.1 Acute toxicity: Oral | 2008e | Etude de la toxicité orale aigue chez le rat - Méthode par classe de toxicité Aiguë - OCDE 423 - Element d'essai: Spray 2 en 1 apaisant répulsif anti moustiques - Ref 096587. Study report n° To 389/08-2817. GLP. | Yes | LABORATOIRES JUVA SANTE |  |

## Output tables from exposure assessment tools

**References used for the exposure assessment:**

HEEG 17 (2013) Default human factor values for use in exposure assessments for biocidal products. Endorsed at TM II 2013.

US EPA (2011) Exposure Factors Handbook: 2011 Edition. EPA/600/R-090/052F. 1436 pages.

H.J. Bremmer, W.M. Blom, P.H. van Hoeven-Arentzen, L.C.H. Prud’homme de Lodder, M.T.M. van Raaij, E.H.F.M. Straetmans, M.P. van Veen, J.G.M. van Engelen (2006) Pest Control Products Fact Sheet To assess the risks for the consumer - Updated version for ConsExpo 4. RIVM report 320005002/2006, p 80.

L.C.H. Prud’homme de Lodder, H.J. Bremmer, J.G.M. van Engelen (2006) Cleaning Products Fact Sheet To assess the risks for the consumer. RIVM report 320104003/2006, p 119.

RIVM (2010) New default values for the spray model. p 4.

**Default human factor values and value considered for application / exposure assessment**

***Body surface - adult (female, 30 to <40 years old, 25th percentile – HEEG 2013, US EPA 2011).***

Tableau 1: Body parts (X) and surfaces considered for the exposure assessment for adults.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Body parts** | | | **Scenarios 1 & 2** | **Scenario 3** | **Scenario 4** |
| Total | | 16600 cm² | 8965 cm² | 8045 cm² | 9420 cm² |
| Head/face | Head | 1110 cm² |  |  |  |
| Face\* | 555 cm² | X |  | X |
| Trunck | Neck\*\* | 455 cm² |  | X | X |
| Trunck | 2270 cm² |  |  |  |
| Legs | Thighs | 3190 cm² | X | X | X |
| Legs | 2130 cm² | X | X | X |
| Feet | Feet | 1130 cm² |  |  |  |
| Arms | Upper Arms | 1141 cm² | X | X | X |
| Lower Arms | 1129 cm² | X | X | X |
| Hands | Hands | 820 cm² | X |  | X |

*\* Face surface is considered to be 50% of the head surface*

*\*\* In the US EPA Exposure Factors Handbook, the surface of the neck is included in the trunck surface. The value of 455 cm² (n=7) is extracted from Cross et al. (2010)[[7]](#footnote-7).*

***Body surface - child (female, 3 years old, 25th percentile – HEEG 2013, US EPA 2011).***

Tableau 2: Body parts (X) and surfaces considered for the exposure assessment for children (3 years).

| **Body parts** | | | | **Scenarios 1 & 2** | **Scenario 3** | **Scenario 4** |
| --- | --- | --- | --- | --- | --- | --- |
| Total | | 100%\* | 6800 cm²\*\* | 3013 cm² | 2993 cm² | 3261 cm² |
| Head/face | Head | 7.8 | 537 cm² |  |  |  |
| Face | 3.9 | 268 cm² | X |  | X |
| Trunck | Neck | 3.6 | 248 cm² |  | X | X |
| Bosom | 12.6 | 867 cm² |  |  |  |
| Shoulders | 2 | 138 cm² |  |  |  |
| Abdomen | 2.9 | 200 cm² |  |  |  |
| Back | 13.4 | 922 cm² |  |  |  |
| Genitals and  Buttocks | Genitals and  Buttocks | 6.6 | 454 cm² |  |  |  |
| Legs | Thighs | 15.6 | 1073 cm² | X | X | X |
| Legs | 10.4 | 716 cm² | X | X | X |
| Feet | Feet | 6.3 | 433 cm² |  |  |  |
| Arms | Upper Arms | 8.4 | 578 cm² | X | X | X |
| Lower Arms | 5.5 | 378 cm² | X | X | X |
| Hands | Hands | 4.9 | 337 cm² |  |  |  |

*\* Values from Table 7-8 of US EPA (2011) (female – Age 4 years old)*

*\*\* Total body surface from Table 7-9 of US EPA (2011) (female – Age 3 to 6 years – 25th percentile as recommened in HEEG 17 (2013). Body part surfaces are from the mean portions (%) multiplied by the total body surface.*

*Other default human factors*

|  |  |  |
| --- | --- | --- |
| **Human factors** | **Adults** | **Children (3 years)** |
| Body weight (kg) | 60 kg\* | 15.6 kg\*\* |
| Short-term exposure values for inhalation (m3/h) | 1.25 m3/h | -\*\*\* |

*\* From HEEG Opinion 17 (2013)*

*\*\* Bodyweight from Table 8-5 of US EPA (2011) (female, Age 3 to 6 years – 25th percentile as recommened in HEEG 17 (2013).*

*\*\*\* Not used for the risk assessment as long as the application of the biocidal products is done by adult only, and application directly on the face is not allowed*New information on the active substance

Not relevant – no additional information available on the active substance.

## Residue behaviour

Not relevant – no residue has to be assessed.

## Summaries of the efficacy studies (B.5.10.1-xx)

The applicant has submitted following efficacy studies for the Meta SPC 1 (aerosol application):

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Experimental data on the efficacy of the biocidal product against target organism(s)** | | | | | | | |
| **Function** | **Field of use envisaged** | **Test substance** | **Test organism(s)** | **Test method** | **Test system / concentrations applied / exposure time** | **Test results: effects** | **Reference** |
| Repellent | skin application | **Marie rose aerosol protection antimoustique**  Réf. 096560  Aerosol formulation without propellant gaz  => 14% IR3535 | *Aedes aegypti*  *Ae. albopictus*  *Culex pipiens*  *Anopheles gambiae*  200 adult females / cages of 64000 cm3 | WHO/HTM/NTD/WHOPES/2009.4 | Arm in cage  **1 g per 600 cm² => 16.67 g/m²**  3 minutes repeated every hour until the first landing and then every 30 minutes until proven inefficacy of the product.  10 volunteers  Normal conditions :  27°C 65%RH (Culex)  Tropical conditions 32°C 75% RH (*Anopheles* and *Aedes*) | Test item has proved a complete protection over a period of:  - 8H against *Ae. aegypti*, *Cx. pipiens*;  - 7,5H against *Ae. albopictus,* *An. gambiae*.  **Tested dose is not the claimed dose** | Serrano, 2015a  RI = 1 |
| Repellent | skin application | **Marie rose aerosol protection antimoustique**  Réf. 096560  Aerosol formulation without propellant gaz  => 13.8% IR3535 | *Ae. albopictus*  *An. gambiae*  *P. duboscqi*  200 adult females / cages of 64000 cm3 | WHO/HTM/NTD/WHOPES/2009.4 | Arm in cage  **0.35 g per 600 cm² => 5.83 g/m²**  5 minutes repeated every hour until the first landing and then every 30 minutes until proven inefficacy of the product.  10 volunteers  Tropical conditions 32°C 75% RH | Test item has proved a complete protection over a period of:  - 7.5H against *Ae. albopictus, P. duboscqi*;  - 7H against *An. gambiae*. | Serrano, 2015b  RI = 1 |

For the Meta SPC 2 (spray application), the applicant has submitted following data:

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Experimental data on the efficacy of the biocidal product against target organism(s)** | | | | | | | |
| **Function** | **Field of use envisaged** | **Test substance** | **Test organism(s)** | **Test method** | **Test system / concentrations applied / exposure time** | **Test results: effects** | **Reference** |
| Repellent | skin application | **Marie Rose Spray anti-moustiques –** Réf. 096602  Spray formulation 20% IR3535 | *Ae. aegypti*  *Ae. albopictus*  *Cx. pipiens*  *An. gambiae*  *P. duboscqi*  200 adult females / cages of 64000 cm3 | WHO/HTM/NTD/WHOPES/2009.4 | Arm in cage  **Application rate: 0.35g per 600 cm² => 5.83 g/m²**  5 minutes repeated every hour until the first landing and then every 30 minutes until proven inefficacy of the product.  10 volunteers  Normal conditions :  27°C 65%RH (Culex)  Tropical conditions 32°C 75% RH (*Phlebotomus*, *Anopheles* and *Aedes*) | Test item has proved a complete protection over a period of:  - 6.5H against *Ae. aegypti,* *An. gambiae;*  - 7H against *Ae. albopictus, P. duboscqi;*  - 7.5H against *Cx. pipiens.* | *Serrano, 2016a*  RI = 1 |
| Repellent | skin application | **Marie Rose Spray anti-moustiques –** Réf. 096602  Spray formulation 20% IR3535 | *Ixodes ricinus*  5 adults and 5 nymphs per mouse  10 mice | Derivated from OPPTS 810.3700 (2010) | Ticks placed on an untreated zone 3 cm away from the treated mouse  **Application rate: 0,033 g / 44 cm² => 7.5 g/m²**  Records of the number of ticks crossing the separating line between the untreated area and the treated skin part.  Test conditions :  25°C 65%RH | Test item has proven a protection over a period of 6 hours against the adults (6.1h) and nymphs (6.3h) of the tick *Ixodes ricinus*. | *Serrano, 2016b*  RI = 2 |

## Confidential annex

For confidential annex, see separated document.

## Information on the substance(s) of concern

Denatured alcohol (EtOH 50-100% with propan-2-ol 5% and 2-methylpropan-2-ol 0.1%) is a substance of concern for the meta SPC 1 and propan-2-ol present in this mixture isna substance of concern for the meta SPC 2.

## Other

Not relevant.

1. Please fill in here the identifying product name from R4BP. [↑](#footnote-ref-1)
2. ECHA (2015) Guidance on the Biocidal Products Regulation - Volume III Human Health - Part B Risk Assessment - Version 1.1 - April 2015 [↑](#footnote-ref-2)
3. http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d8b4df8-d70a-6e6b-e044-00144f67d249/DISS-9d8b4df8-d70a-6e6b-e044-00144f67d249\_DISS-9d8b4df8-d70a-6e6b-e044-00144f67d249.html (Acceded on 12 October, 2015). [↑](#footnote-ref-3)
4. Proposal for harmonising the assessment of human exposure to repellents (PT19) Agreed at the HH WH III 2016 [↑](#footnote-ref-4)
5. HEEG opinion 17: US EPA Exposure Factors Handbook (2011 Issue), which are derived from US EPA Analysis of NHANES 1999-2006 [↑](#footnote-ref-5)
6. Dilution factor from ConsExpo 4.0, Consumer Exposure and Uptake Models. Program Manuel. Bilthoven, The Netherlands: National Institute for Public Health and the Environment (RIVM). Report no. 320104004. & RIVM report 320104001/2006 : Cosmetics Fact Sheet To assess the risks for the consumer (Updated version for ConsExpo 4) H.J. Bremmer, L.C.H. Prud’homme de Lodder, J.G.M. van Engelen [p34 : "Weight fraction dilution Wf / 3" " Estimate dilution factor 3 (wetting hands)] [↑](#footnote-ref-6)
7. Cross A, Collard M, Nelson A (2008) Body Segment Differences in Surface Area, Skin Temperature and 3D Displacement and the Estimation of Heat Balance during Locomotion in Hominins. PLOS. **Vol 3**, 6, e2464, pp 1-9. [↑](#footnote-ref-7)